Novel Nitrogen-Containing Heterocyclic Compounds

Background

The present disclosure relates to novel compounds. The disclosure also relates to the preparation of the compounds and intermediates used in the preparation, compositions containing the compounds, and uses of the compounds including their use as a STAT6 inhibitor.

STAT6 is a member of the Signal Transducer and Activator of Transcription (STAT) family of proteins consisting of transcription factors that impact cell processes including differentiation, survival, proliferation, and functional activation [Levy, DE and Darnell, JE. *STATs: transcriptional control and biological impact*. 2002. Nat Rev Mol Cell Biol. 3(9):651–62]. The STAT family consists of seven members: STAT1, STAT2, STAT3, STAT4, STAT5a, STAT5b, and STAT6.

STAT family proteins are downstream targets of the Janus kinase (JAK) family kinases, which contribute to signal transduction from a variety of cytokines including IL-2, IL-5, GM-CSF, IL-10, IL-12, IL-23, as well as IL-4 and IL-13. Cytokines IL-4 and IL-13 have been demonstrated to signal through STAT6 activation [Kaplan, MH et al. 1996. *Stat6 is required for mediating responses to IL-4 and for development of Th2 cells*. Immunity. 4: 313-319]. The pathogenic activity of IL-4 and IL-13 cytokines is consistent with efficacy that has been observed with JAK inhibitors, which block signaling of IL-4 and IL-13 as well as signaling of additional inflammatory cytokines [Simpson, EL et al. 2020. *Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial*. Lancet. 396(10246): 255-266; Guttman-Yassky, E et al. 2021. *Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials*. Lancet. 397(10290): 2151-2168].

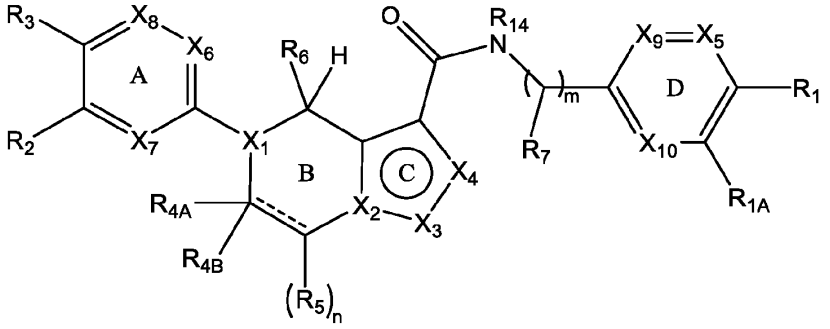
Despite the effectiveness of known therapeutics, an unmet need remains for safe and effective therapeutics for numerous diseases characterized by inflammatory responses, that address a broad range of pathogenic mechanisms.

Brief Summary

The present disclosure provides, in part, compounds and pharmaceutically acceptable salts thereof. Such compounds may inhibit the activity of STAT6 and may be useful in the treatment, prevention, suppression, and/or amelioration of disease(s), disorders and conditions mediated by STAT6. Also provided are pharmaceutical compositions, comprising the compounds or salts, alone or in combination with additional therapeutic agents. The present disclosure also provides, in part, methods for preparing such compounds, pharmaceutically

acceptable salts and compositions of the disclosure, and methods of using the foregoing. This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the detailed description. This summary is not intended to identify key features or essential features of the claimed subject matter, nor is it intended to be used in isolation as an aid in determining the scope of the claimed subject matter.

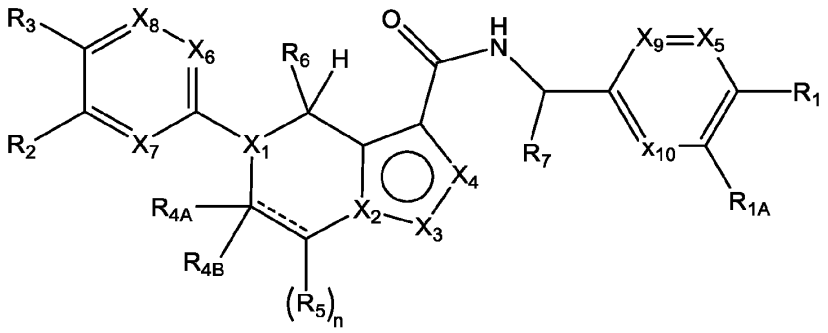
In an aspect, a compound of the disclosure has the Formula I or a pharmaceutically acceptable salt thereof:



I

where the variables are defined herein.

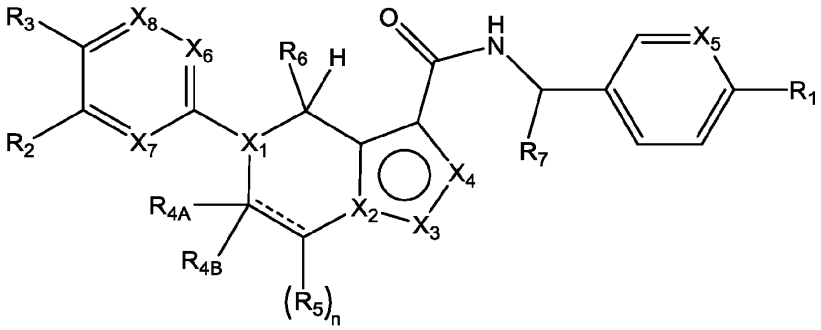
In an aspect, a compound of the disclosure has the Formula IA or a pharmaceutically acceptable salt thereof:



IA

where the variables are defined herein.

In an aspect, a compound of the disclosure has the Formula IB or a pharmaceutically acceptable salt thereof:



IB

where the variables are defined herein.

In an aspect, the disclosure relates to a pharmaceutical composition comprising a compound of the disclosure, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

In another aspect, the disclosure relates to a method for treating atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease, chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa comprising administering to a subject in need thereof a therapeutically effective amount of the compound of the disclosure.

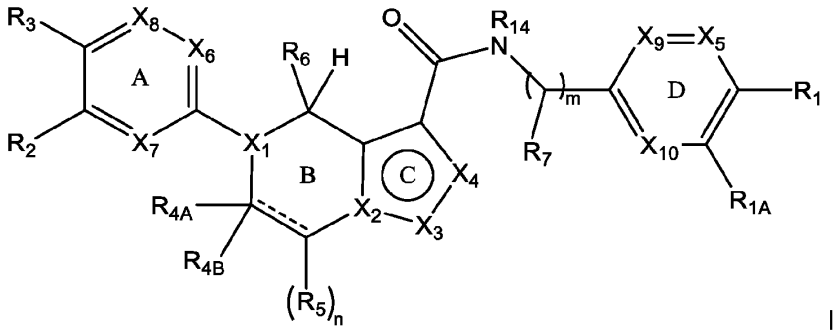
In another aspect, the disclosure relates to the compound of the disclosure or a pharmaceutically acceptable salt thereof for use as a medicament; or for use in the treatment of atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease (COPD), chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), a joint disorder, keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa; or for use in the treatment of at least one of a dermatological condition or a respiratory condition.

It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the disclosure, as claimed.

Detailed Description

The present disclosure may be understood more readily by reference to the following detailed description and the Examples included herein. It is to be understood that this disclosure is not limited to specific synthetic methods of making that may of course vary. It is to be also understood that the terminology used herein is for the purpose of describing specific aspects only and is not intended to be limiting.

In an aspect, a compound of Formula I or a pharmaceutically acceptable salt thereof:



I

wherein

X_1 is CH, CNH_2, or N;

X_2 is C or N;

X_3 is CR_{13}, N, NR_{13}, O, or S;

X_4 is CH, N, or NR_{13};

X_5 is CR_{1B} or N;

X_6 is CH or N;

X_7 is CH, N, or CF;

X_8 is CH or N;

X_9 is CR_{1B} or N;

X_{10} is CR_{1B} or N;

R_1 is $-NHR_8$, -OH, $-C_{2-5}$ heterocycle, or $-C_{1-3}$ alkyl; wherein the $-C_{2-5}$ heterocycle of R_1 is optionally substituted with one, two, or three of $-C_{1-3}$ alkyl, $-C_{1-3}$ oxoalkyl, $-C_{3-5}$ heterocycloalkyl, $-C_{3-5}$ hydroxyheterocycloalkyl, $-C_{3-5}$ aminoheterocycloalkyl, or oxo; wherein the $-C_{1-3}$ alkyl of R_1 is optionally substituted with one, two, or three of oxo, $-NR_{10A}R_{11}$, or $-NR_{10}R_{11}$;

R_{1A} is H, halogen, or $-CH_3$; or

R_1 and R_{1A} form a C_{5-7} heterocycloalkyl fused to Ring D or a C_{5-7} heteroaryl fused to Ring D; wherein the C_{5-7} heterocycloalkyl or the C_{5-7} heteroaryl is optionally substituted with oxo;

each R_{1B} independently is H, $-CH_3$, F, Cl, or methoxy;

R_2 is H, $-C_{1-3}$ alkyl, $-C_{1-3}$ alkoxy, $-C_{1-3}$ fluoroalkyl, or halogen;

R_3 is $-C_{1-3}$ alkyl, $-C_{2-10}$ heterocycle, $-P(=O)(CH_3)_2$, $-S(=O)CH_3$, $-NH-S(=O)_2CH_3$, or $-NH-C(=O)-C_{1-3}$ alkyl; wherein the $-C_{1-3}$ alkyl of R_3 is optionally substituted with one, two, or three of oxo, halogen, $-C_{3-6}$ cycloalkyl, -OH, $-NR_{12}R_{12A}$, or cyano; wherein the $-C_{2-10}$ heterocycle is optionally substituted with one, two, or three of -OH, halogen, $-C_{1-3}$ hydroxyalkyl, $-C_{1-3}$ alkoxy, $-C_{1-3}$ alkyl, $-C_{1-3}$ fluoroalkyl, cyclopropyl, or oxo; or

R_2 and R_3 form a C_{3-6} heterocycle fused to Ring A optionally substituted with one, two, or three of $-C_{1-3}$ alkyl, $-C_{2-3}$ oxoalkyl, or oxo;

R_{4A} is H, -OH, $-C_{1-3}$ fluoroalkyl, or $-C_{1-3}$ alkyl;

R_{4B} is H or is absent; or

R_{4A} and R_{4B} form cyclopropyl;

each R_5 independently is H, halogen, -OH, cyclopropyl, -C_{1-3} fluoroalkyl, or -C_{1-3} alkyl; or two R_5 groups form cyclopropyl;

R_6 is H, -OH, or -C_{1-3} alkyl; or

R_{4A} and R_6 or one R_5 and R_6 form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge; or

R_{4B} and one R_5 form a C_{3-5} cycloalkyl fused to Ring B; R_7 is H, -C_{1-3} alkyl, or -C_{1-3} hydroxyalkyl;

R_8 is H, -C_{1-3} alkyl, -SO_2CH_3, or a -C_{3-4} heterocycle; wherein the -C_{1-3} alkyl of R_8 is optionally substituted with one, two, or three of oxo, -C_{3-9} heterocycloalkyl, -C_{1-3} alkoxy, cyanoimine, or -NR_9R_{10}; wherein the -C_{3-4} heterocycle of R_8 is optionally substituted with one, two, or three of oxo, halogen, -C_{0-1} alkylene-$NR_{10}R_{11}$, -OH, -C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy optionally substituted with -$NR_{10}R_{11}$, -C_{1-3} alkyl-C_{1-3} alkoxy, -C_{1-3} oxoalkyl, or -C_{1-3} alkyl; wherein the -C_{3-9} heterocycloalkyl of R_8 is optionally substituted with one, two, or three of -C_{1-3} alkyl, -OH, -C_{1-3} hydroxyalkyl, -O-C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy, -C_{1-3} alkyl-C_{1-3} alkoxy, halogen, -C_{1-3} fluoroalkyl, -C_{1-3} fluoroalkoxy, cyano, -C_{1-3} cyanoalkyl, -C_{0-1} alkylene-C_{3-5} heterocycloalkyl, -O-C_{3-5} heterocycloalkyl, or -C_{0-1} alkylene-$NR_{10}R_{11}$;

R_9 is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_9 is optionally substituted with one, two, or three of -C_{3-5} cycloalkyl, -C_{3-5} heterocycloalkyl, or methoxy; wherein the -C_{3-5} cycloalkyl of R_9 is optionally substituted with one or two of -OH or -C_{1-3} alkyl;

each R_{10} independently is H or -C_{1-4} alkyl; or

R_{10A} is -C_{0-1} alkylene-C_{3-5} heterocycloalkyl optionally substituted with -C_{1-3} alkyl;

each R_{11} independently is H or -C_{1-3} alkyl;

R_{12} is H, -C_{1-3} alkyl, -C_{1-3} hydroxyalkyl, -$(CH_2)_{0-2}$-C_{3-5} heterocycloalkyl, -$(CH_2)_{1-2}$-O-C_{3-5} heterocycloalkyl, -methylene-C(=O)-$NR_{10}R_{11}$, or -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$; wherein the -$(CH_2)_{0-2}$-C_{3-5} heterocycloalkyl or the -$(CH_2)_{1-2}$-O-C_{3-5} heterocycloalkyl of R_{12} is optionally substituted with -C_{1-4} alkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, -$(CH_2)_{0-1}$-phenyl, halogen, -C_{1-3} fluoroalkyl, or -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl; wherein the -C_{1-3} alkyl of R_{12} is optionally substituted with one, two, or three of oxo or $NR_{10}R_{11}$;

R_{12A} is H or -C_{1-4} alkyl; or

R_{12} and R_{12A} form a C_{3-10} heterocycle optionally substituted with one, two, or three of -OH, -C_{1-3} alkyl, oxo, halogen, -C_{2-3} oxoalkyl, -C_{1-3} alkoxy, -C_{1-3} hydroxyalkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, cyano, -C_{3-6} cycloalkyl, -$S(=O)_2CH_3$, -$S(=O)_2CH_2CH_3$, -C(=O)-$NR_{10}R_{11}$, or -$NHC(=O)CH_3$;

R_{13} is H, -C_{1-6} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, -C_{1-4} cyanoalkyl, -C_{3-5} cycloalkyl, -C_{2-4} oxoalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-6} alkyl of R_{13} is optionally substituted with one, two, or three of oxo, fluoro, -NH_2, C_{3-6} cycloalkyl, or methoxy;

wherein the -C_{3-5} cycloalkyl or the -C_{3-6} cycloalkyl of R_{13} is optionally substituted with one, two, or three of -C_{1-3} alkyl, -C_{1-3} fluoroalkyl, or halogen;

R_{14} is H; or

X_4 is NR_{13} and R_{13} and R_{14} form a C_{4-5} heterocycle fused to Ring C;

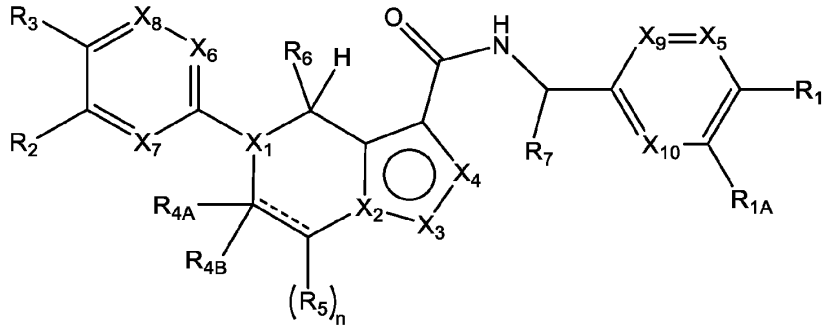
n is 1 or 2;

m is 0 or 1;

wherein if X_3 is CR_{13} or NR_{13} then X_4 is CH or N, and if X_4 is NR_{13} then X_3 is N, O, or S;

wherein the respective heterocycles each independently include 1 to 4 heteroatoms including at least one of N, O, or S.

In an aspect, a compound of Formula IA or a pharmaceutically acceptable salt thereof:



IA

wherein

X_1 is CH, CNH_2, or N;

X_2 is C or N;

X_3 is CR_{13}, N, NR_{13}, O, or S;

X_4 is CH, N, or NR_{13};

X_5 is CH, CR_{1B}, or N;

X_6 is CH or N;

X_7 is CH, N, or CF;

X_8 is CH or N;

X_9 is CH, CR_{1B}, or N;

X_{10} is CH, CR_{1B}, or N;

R_1 is -NHR_8, -OH, -C_{2-5} heterocycle, or -C_{1-3} alkyl; wherein the -C_{2-5} heterocycle of R_1 is optionally substituted with one, two, or three of -C_{1-3} alkyl, -C_{1-3} oxoalkyl, -C_{3-5} heterocycloalkyl, -C_{3-5} hydroxyheterocycloalkyl, -C_{3-5} aminoheterocycloalkyl, or oxo; wherein the -C_{1-3} alkyl of R_1 is optionally substituted with one, two, or three of oxo or -$NR_{10}R_{11}$;

R_{1A} is H or -CH_3; or

R_1 and R_{1A} form a C_{6-8} fused heterocycloalkyl or a C_{6-8} fused heteroaryl; wherein the C_{6-8} fused heterocycloalkyl or the C_{6-8} fused heteroaryl is optionally substituted with oxo;

each R_{1B} independently is H, -CH_3 , F, Cl, or methoxy;

R_2 is H, -C_{1-3} alkyl, -C_{1-3} fluoroalkyl, or halogen;

R_3 is -C_{1-3} alkyl, -C_{2-10} heterocycle, or -NH-C(=O)-C_{1-3} alkyl; wherein the -C_{1-3} alkyl of R_3 is optionally substituted with one or more of oxo, -OH, -$NR_{12}R_{12A}$, -C_{5-8} heterocycle, or cyano; wherein the -C_{2-10} heterocycle is optionally substituted with one, two, or three of -OH, halogen, -C_{1-3} hydroxyalkyl, -C_{1-3} alkyl, cyclopropyl, or oxo; or

R_2 and R_3 form a C_{6-10} fused heterocycle optionally substituted with one, two, or three of -C_{1-3} alkyl, -C_{2-3} oxoalkyl, or oxo;

R_{4A} is H, -OH, or -C_{1-3} alkyl;

R_{4B} is H or is absent;

each R_5 independently is H, halogen, -OH, cyclopropyl, or -C_{1-3} alkyl; or two R_5 groups form cyclopropyl;

R_6 is H, -OH, or -C_{1-3} alkyl; or

R_{4A} and R_6 or R_5 and R_6 form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge;

R_7 is H, -C_{1-3} alkyl, or -C_{1-3} hydroxyalkyl;

R_8 is H, -C_{1-3} alkyl, -SO_2CH_3, or a -C_{3-4} heterocycle; wherein the -C_{1-3} alkyl of R_8 is optionally substituted with one, two, or three of oxo, -C_{3-7} heterocycloalkyl, -C_{3-7} heterocycloalkyl substituted with methyl, alkoxy, cyanoimine, or -NR_9R_{10}; wherein the -C_{3-4} heterocycle is optionally substituted with one, two, or three of oxo, halogen, -C_{0-1} alkylene-$NR_{14}R_{11}$, -OH, -C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy optionally substituted with -$NR_{10}R_{11}$, -C_{1-3} alkoxy-C_{1-3} alkyl, -C_{1-3} oxoalkyl, or -C_{1-3} alkyl;

R_9 is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_9 is optionally substituted with one, two, or three of cyclopropyl, -C_{3-5} heterocycloalkyl, or methoxy; wherein the -C_{3-5} cycloalkyl of R_9 is optionally substituted with -C_{1-3} alkyl;

each R_{10} independently is H or -C_{1-4} alkyl; or

if the -C_{1-3} alkyl of R_8 is substituted with -NR_9R_{10}, then the corresponding R_9 and R_{10} are optionally combined to form a C_{3-7} heterocycloalkyl optionally substituted with at least one of methoxy, OH, -C_{1-3} alkyl, halogen, -NH_2, -$NHCH_3$, or -$N(CH_3)_2$;

each R_{11} independently is H or -C_{1-3} alkyl;

R_{12} is H, -C_{1-3} alkyl, -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl, or -methylene-phenylene-NH-C-$NR_{10}R_{11}$; wherein the -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl is optionally substituted with -C_{1-4} alkyl;

R_{12A} is H or -C_{1-4} alkyl; or

R_{12} and R_{12A} form a fused C_{5-10} heterocycloalkyl optionally substituted with -C_{1-3} alkyl;

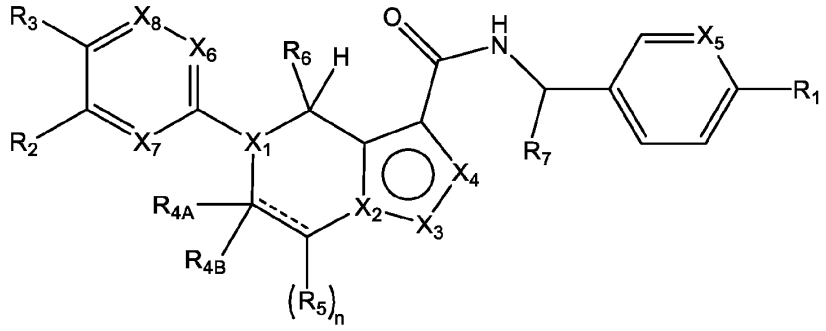
R_{13} is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{0-1}-C_{3-5} cycloalkyl, -C_{2-4} oxoalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_{13} is optionally substituted with one, two, or three of cyclopropyl or methoxy; wherein the -C_{3-5} cycloalkyl of R_{13} is optionally substituted with -C_{1-3} alkyl;

n is 1 or 2;

wherein the respective heterocycles each independently include 1 to 3 heteroatoms including at least one of N, O, or S;

wherein at least one of X_2 is N or X_3 is N, NH, or NR_{13}, and X_4 is N or NR_{13}; or if X_3 is S or O, then X_2 is C.

In an aspect, a compound has the Formula IB or a pharmaceutically acceptable salt thereof:



IB

wherein

X_1 is CH, CNH_2, or N;

X_2 is C or N;

X_3 is CR_{13}, N, NR_{13}, O, or S;

X_4 is CH, N, or NR_{13};

X_5 is CH or N;

X_6 is CH or N;

X_7 is CH, N, or CF;

X_8 is CH or N;

with the proviso that at least one of X_2 is N or X_3 is N, NH, or NR_{13}, and X_4 is N or N R_{13}; or if X_3 is S or O, then X_2 is C;

R_1 is $-NHR_8$, OH, $-C_{2-5}$ heterocycle, or $-C_{1-3}$ alkyl; wherein the $-C_{2-5}$ heterocycle of R_1 is optionally substituted with one or more of $-C_{1-3}$ alkyl, $-C_{1-3}$ oxoalkyl, $-C_{3-5}$ heterocycloalkyl, $-C_{3-5}$ hydroxyheterocycloalkyl, $-C_{3-5}$ aminoheterocycloalkyl, or oxo; wherein the $-C_{1-3}$ alkyl of R_1 is optionally substituted with one or more of oxo or $-NR_{10}R_{11}$;

R_2 is H, $-C_{1-3}$ alkyl, $-C_{1-3}$ fluoroalkyl, or halogen;

R_3 is $-C_{1-3}$ alkyl, $-C_{2-10}$ heterocycle, or -NH-C(=O)-C_{1-3} alkyl; wherein the $-C_{1-3}$ alkyl of R_3 is optionally substituted with one or more of oxo, -OH, $-NR_{12}R_{12A}$, $-C_{5-8}$ heterocycle, or cyano; wherein the $-C_{2-10}$ heterocycle is optionally substituted with one or more of -OH, halogen, $-C_{1-3}$ hydroxyalkyl, $-C_{1-3}$ alkyl, cyclopropyl, or oxo; or

R_2 and R_3 form a C_{6-10} fused heterocycloalkyl optionally substituted with one or more of $-C_{1-3}$ alkyl, $-C_{2-3}$ oxoalkyl, or oxo;

R_{4A} is H, -OH, or $-C_{1-3}$ alkyl;

R_{4B} is H or is absent;

each R_5 independently is H, -OH, halogen, or -C_{1-3} alkyl; or two R_5 groups form cyclopropyl;

R_6 is H, -OH, or -C_{1-3} alkyl; or

R_{4A} and R_6 or R_5 and R_6 form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge;

R_7 is H, -C_{1-3} alkyl, or -C_{1-3} hydroxyalkyl;

R_8 is H, -C_{1-3} alkyl, or a -C_{3-4} heterocycle; wherein the -C_{1-3} alkyl of R_8 is optionally substituted with one or more of oxo or -NR_9R_{10}; wherein the -C_{3-4} heterocycle is optionally substituted with one or more of oxo or -C_{1-3} alkyl;

R_9 is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_9 is optionally substituted with one or more of cyclopropyl, -C_{3-5} heterocycloalkyl, or methoxy; wherein the -C_{3-5} cycloalkyl of R_9 is optionally substituted with -C_{1-3} alkyl;

each R_{10} independently is H or -C_{1-4} alkyl; or

if the -C_{1-3} alkyl of R_8 is substituted with -NR_9R_{10}, then the corresponding R_9 and R_{10} are optionally combined to form a C_{3-6} heterocycloalkyl optionally substituted with at least one of methoxy, OH, -C_{1-3} alkyl, or -$N(CH_3)_2$;

each R_{11} independently is H or -C_{1-3} alkyl;

R_{12} is H, -C_{1-3} alkyl, or -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$;

each R_{13} independently is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_{13} is optionally substituted with one or more of cyclopropyl or methoxy; wherein the -C_{3-5} cycloalkyl of R_{13} is optionally substituted with -C_{1-3} alkyl;

n is 1 or 2; and

wherein the respective heterocycles each independently include 1 to 3 heteroatoms including at least one of N, O, or S.

In an aspect, R_3 is -C_{1-3} alkyl or -C_{2-10} heterocycle; the -C_{2-10} heterocycle is -C_{2-5} heteroaryl; the -C_{1-3} alkyl of R_3 is optionally substituted with one, two, or three of oxo or -$NR_{12}R_{12A}$; and the -C_{2-5} heterocycle of R_3 is optionally substituted with -C_{1-3} alkyl.

In an aspect, the dashed line refers to the bond being a single bond or a double bond; if the dashed line is a double bond, then R_{4B} is absent and n is 1.

In an aspect, R_1 is -NHR_8; and R_8 is -C_{1-3} alkyl substituted with one, two, or three of oxo or -NR_9R_{10}.

In an aspect, R_2 is H; and R_3 is -C_{1-3} alkyl substituted with oxo and -$NR_{12}R_{12A}$.

In an aspect, at least one of X_5 is CH; X_7 is CH or N; X_8 is CH; R_1 is -NHR_8, -C_{2-5} heterocycle, or -C_{1-3} alkyl; R_{4A} is H or -C_{1-3} alkyl; each R_5 independently is H, halogen, or -C_{1-3} alkyl; or the two R_5 groups form cyclopropyl; R_6 is H or -C_{1-3} alkyl; or R_7 is H or -C_{1-3} alkyl.

In an aspect, R_3 is -C_{1-3} alkyl substituted with oxo and -$NR_{12}R_{12A}$ and R_1 is -NHR_8 or -C_{1-3} alkyl substituted with oxo and -$NR_{10}R_{11}$.

In an aspect, R3 can be -C(=O)-$NR_{12}R_{12A}$ and R1 can be -NH-CO-$NR_{10}R_{11}$.

In an aspect, X_3 is CR_{13} and X_4 is CH or N.

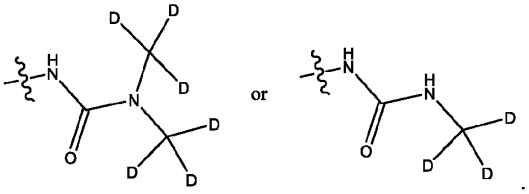
In an aspect, R_1 is -NHR_8; wherein R_8 is -C_{1-3} alkyl or a -C_{3-4} heterocycle; wherein the -C_{1-3} alkyl of R_8 is substituted with oxo and -NR_9R_{10}; wherein the -C_{3-4} heterocycle is substituted with one, two, or three of oxo or -C_{1-3} alkyl.

In an aspect, X_1 is N, X_3 is N or NR_{13}, and X_4 is N.

In an aspect, the -C_{2-6} heterocycle of R_3 is a -C_{2-10} heterocycle and R_3 is optionally substituted with one, two, or three of -C_{1-3} alkyl.

In an aspect, at least one hydrogen (H) is deuterium (D).

In an aspect, R_1 is



In an aspect, R_{1A} is deuterium; X_5, X_9, and X_{10} are each CR_{1B}; and the R_{1B} of each of X_5, X_9, and X_{10} is deuterium.

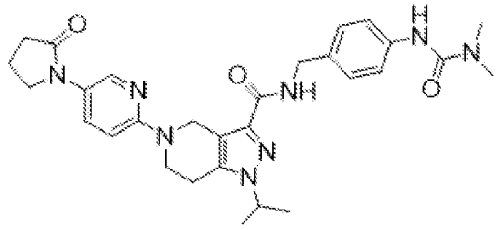
In an aspect, the compound is a deuterated compound of any of Examples D1, D2, D6, D31, D33, D128, or D132.

In an aspect, a compound or a pharmaceutically acceptable salt thereof wherein the compound is one of: *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; 5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; 5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; 5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; (*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-N-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-c]pyridine-3-carboxamide; or 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

In an aspect, a compound wherein the compound is one of: *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; 5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; 5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-

dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; 5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; (*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-N-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-c]pyridine-3-carboxamide; or 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

In an aspect, a compound or a pharmaceutically acceptable salt thereof is

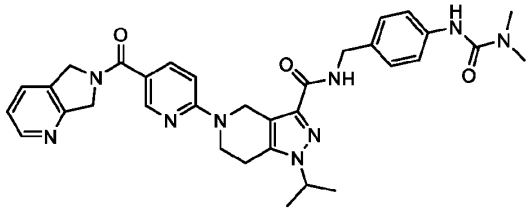


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In an aspect, a compound or a pharmaceutically acceptable salt thereof is

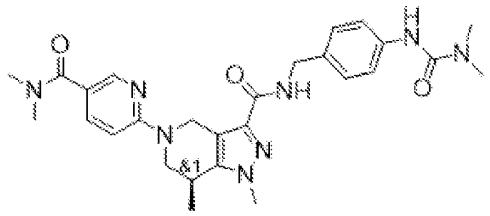
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In an aspect, a compound or a pharmaceutically acceptable salt thereof is

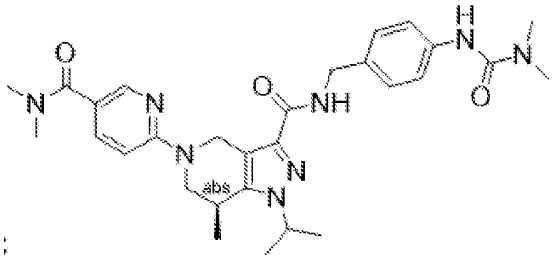


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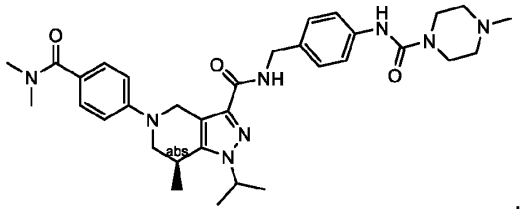
In an aspect, a compound or a pharmaceutically acceptable salt thereof is



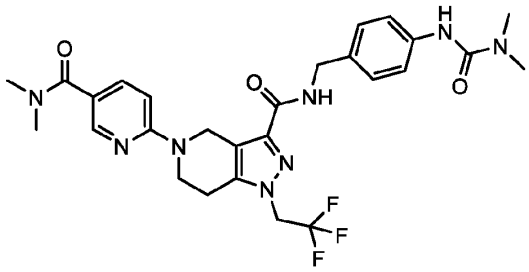
In an aspect, a compound or a pharmaceutically acceptable salt thereof is



In an aspect, a compound or a pharmaceutically acceptable salt thereof is



In an aspect, a compound or a pharmaceutically acceptable salt thereof is



In an aspect, the compound is other than the following: *rac*-(4*R*,7*S*)-9-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-1,4,5,6,7,8-hexahydro-4,7-epiminocyclohepta[*c*]pyrazole-3-carboxamide, *rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(5-(hydroxymethyl)-2-oxooxazolidin-3-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide, *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-((1*S*,4*S*)-6-oxo-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide, *rel*-(*R* or *S*)-*N*-(4-(3,3-

dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide, *rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide, or (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

In an aspect, a pharmaceutical composition comprises the compound of Formula I or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

In an aspect, a method for treating atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease, chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa comprises administering to a subject in need thereof a therapeutically effective amount of the compound of Formula I, or a pharmaceutically acceptable salt thereof.

In an aspect, a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use as a medicament.

In an aspect, a compound of Formula I, or a pharmaceutically acceptable salt thereof, can be for use in the treatment of atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease (COPD), chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), a joint disorder, keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa.

In an aspect, a compound of Formula I, or a pharmaceutically acceptable salt thereof, can be for use in the treatment of at least one of a dermatological condition or a respiratory condition.

In an aspect, use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, can be for the manufacture of a medicament for the treatment of atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease (COPD), chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic

kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), a joint disorder, keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa.

In an aspect, use of a compound, or a pharmaceutically acceptable salt thereof, can be for use in the treatment of at least one of a dermatological condition or a respiratory condition.

In an aspect, the compound or a pharmaceutically acceptable salt thereof is selected from the group consisting of the compounds of Examples 1 and 2 and those listed in Table 2.

In an aspect, a method for treating atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease, chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa comprises administering to a subject in need thereof a therapeutically effective amount of the compound of the any of the preceding aspects, or a pharmaceutically acceptable salt thereof. The method can be for treating atopic dermatitis. The method can be for treating

In an aspect, a compound according to any of the preceding aspects, or a pharmaceutically acceptable salt thereof, is for use as a medicament.

In an aspect, a compound according to any of the preceding aspects, or a pharmaceutically acceptable salt thereof, is for use in the treatment of atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease (COPD), chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), a joint disorder, keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa.

In an aspect, a compound according to any of the preceding aspects, or a pharmaceutically acceptable salt thereof, is for use in the treatment of at least one of a dermatological condition or a respiratory condition.

In an aspect, a use of a compound according to any of the preceding aspects, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease (COPD), chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), a joint disorder, keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa.

In an aspect, a use of a compound according to any of the preceding aspects, or a pharmaceutically acceptable salt thereof, is for use in the treatment of at least one of a dermatological condition or a respiratory condition.

Each of the aspects described herein may be combined with any other aspect(s) described herein not inconsistent with the aspect(s) with which it is combined. In addition, any of the compounds described in the Examples, or pharmaceutically acceptable salts thereof, may be claimed individually or grouped together with one or more other compounds of the Examples, or pharmaceutically acceptable salts thereof, for any of the aspect(s) described herein.

Furthermore, each of the aspects described herein envisions within its scope pharmaceutically acceptable salts of the compounds described herein.

Unless otherwise defined herein, scientific and technical terms used in connection with the present disclosure have the meanings that are commonly understood by those of ordinary skill in the art.

The disclosure described herein suitably may be practiced in the absence of any element(s) not specifically disclosed herein.

The compound(s) of the disclosure refers to the compounds of Formula I and Formula IA, where a compound of Formula I can be a compound specifically of Formula IA. One of ordinary skill in the art will appreciate that the compounds of the disclosure include conformational isomers (e.g., cis and trans isomers) and all optical isomers (e.g., enantiomers and diastereomers), racemic, diastereomeric and other mixtures of such isomers, tautomers thereof, where they may exist. One of ordinary skill in the art will also appreciate that the compounds of the disclosure include solvates, hydrates, isomorphs, polymorphs, esters, salt forms, prodrugs, and isotopically labelled versions thereof, where they may be formed. Compounds of the disclosure can include novel intermediates used in the preparation thereof.

As used herein, the singular form "a", "an", and "the" include plural references unless indicated otherwise. For example, "a" substituent includes one or more substituents. The term "or" means "and/or" unless clearly indicated otherwise.

As used herein, the term “about” when used to modify a numerically defined parameter means that the parameter may vary by as much as 10% below or above the stated numerical value for that parameter. For example, a dose of about 5 mg means 5% ± 10%, i.e., it may vary between 4.5 mg and 5.5 mg.

“Optional" or "optionally" means that the subsequently described event or circumstance may, but need not occur, and the description includes instances where the event or circumstance occurs and instances in which it does not.

The terms “optionally substituted” and “substituted or unsubstituted” are used interchangeably to indicate that the particular group being described may have no non-hydrogen substituents (i.e., unsubstituted), or the group may have one or more non-hydrogen substituents (i.e., substituted). If not otherwise specified, the total number of substituents that may be present is equal to the number of H atoms present on the unsubstituted form of the group being described. Where an optional substituent is attached via a double bond, such as an oxo (=O) substituent, the group occupies two available valences, so the total number of other substituents that are included is reduced by two. In the case where optional substituents are selected independently from a list of alternatives, the selected groups may be the same or different. Throughout the disclosure, it will be understood that the number and nature of optional substituent groups will be limited to the extent that such substitutions make chemical sense to one of ordinary skill in the art.

“Halogen” or “halo” refers to fluoro, chloro, bromo, and iodo (F, Cl, Br, I). More specifically, halogen can refer to fluoro and chloro.

“Cyano” refers to a substituent having a carbon atom joined to a nitrogen atom by a triple bond, i.e., -C≡N. “Cyanoimine” refers to a substituent having a carbon atom joined to a nitrogen atom by a double bond and that is bound to a cyano group, i.e., -C(R)=N-C≡N, where R can be a dimethylamino group, i.e., $-C(N(CH_3)_2)=N-C\equiv N$.

"Hydroxy" refers to an -OH group.

“Oxo” refers to a double bonded oxygen (=O).

"Alkyl" refers to a saturated, monovalent aliphatic hydrocarbon radical that has a specified number of carbon atoms, including straight chain or branched chain groups. Alkyl groups may contain, but are not limited to, 1 to 12 carbon atoms (“C_{1-12} alkyl”), 1 to 8 carbon atoms (“C_{1-8} alkyl”), 1 to 6 carbon atoms (“C_{1-6} alkyl”), 1 to 5 carbon atoms (“C_{1-5} alkyl”), 1 to 4 carbon atoms (“C_{1-4} alkyl”), 1 to 3 carbon atoms (“C_{1-3} alkyl”), or 1 to 2 carbon atoms (“C_{1-2} alkyl”). Examples include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, n-heptyl, n-octyl, and the like. Alkyl groups may be optionally substituted, unsubstituted or substituted, as further defined herein. In some instances, substituted alkyl groups are specifically named by reference to the substituent group. For example, “haloalkyl” refers to an alkyl group having the specified number

of carbon atoms that is substituted by one or more halo substituents, up to the available valence number.

"Haloalkyl" refers to an alkyl group as defined above containing the specified number of carbon atoms wherein at least one hydrogen atom has been replaced by halogen. Haloalkyl groups man contain, but are not limited to, 1-6 carbon atoms ("C_{1-6} haloalkyl"), 1-4 carbon atoms ("C_{1-4} haloalkyl"), or 1-2 carbon atoms ("C_{1-2} haloalkyl"). More specifically, fluorinated alkyl groups may be specifically referred to as "fluoroalkyl." Examples of fluoroalkyl groups include, but are not limited to, fluoromethyl, difluoromethyl, fluoroethyl, difluoroethyl, trifluoroethyl, and tetrafluoroethyl. Examples of fully substituted fluoroalkyl groups (also referred to as perfluoroalkyl groups) include trifluoromethyl ($-CF_3$) and pentafluoroethyl ($-C_2F_5$).

"Hydroxyalkyl" refers to an alkyl group as defined above containing the specified number of carbon atoms wherein at least one hydrogen atom has been replaced by hydroxy (OH), for example, only one hydrogen atom is replaced by hydroxy. Hydroxyalkyl groups man contain, but are not limited to, 1-6 carbon atoms ("C_{1-6} hydroxyalkyl"), 1-4 carbon atoms ("C_{1-4} hydroxyalkyl"), or 1-2 carbon atoms ("C_{1-2} hydroxyalkyl").

"Cyanoalkyl" refers to an alkyl group as defined above containing the specified number of carbon atoms wherein at least one hydrogen atom has been replaced by cyano ($-C\equiv N$). Cyanoalkyl groups man contain, but are not limited to, 1-6 carbon atoms ("C_{1-6} cyanoalkyl"), 1-4 carbon atoms ("C_{1-4} cyanoalkyl"), or 1-2 carbon atoms ("C_{1-2} cyanoalkyl").

"Oxoalkyl" refers to an alkyl group as defined above containing the specified number of carbon atoms wherein at least two hydrogen atoms have been replaced by an oxo group. Oxoalkyl groups man contain, but are not limited to, 1-6 carbon atoms ("C_{1-6} oxoalkyl"), 1-4 carbon atoms ("C_{1-4} oxoalkyl"), or 1-2 carbon atoms ("C_{1-2} oxoalkyl").

"Alkoxy" refers to an alkyl group, as defined herein, that is single bonded to an oxygen atom. The attachment point of an alkoxy radical to a molecule is through the oxygen atom. An alkoxy radical may be depicted as alkyl-O-. Alkoxy groups may contain, but are not limited to, 1 to 8 carbon atoms ("C_{1-8} alkoxy"), 1 to 6 carbon atoms ("C_{1-6} alkoxy"), 1 to 4 carbon atoms ("C_{1-4} alkoxy"), or 1 to 3 carbon atoms ("C_{1-3} alkoxy"). Alkoxy groups include, but are not limited to, methoxy, ethoxy, n-propoxy, isobutoxy, and the like.

"Alkylene" refers to a saturated, divalent aliphatic hydrocarbon radical that has a specified number of carbon atoms, including straight chain or branched chain groups. Alkylene groups may contain, but are not limited to, 1 to 12 carbon atoms ("C_{1-12} alkylene"), 1 to 8 carbon atoms ("C_{1-8} alkylene"), 1 to 6 carbon atoms ("C_{1-6} alkylene"), 1 to 5 carbon atoms ("C_{1-5} alkylene"), 1 to 4 carbon atoms ("C_{1-4} alkylene"), 1 to 3 carbon atoms ("C_{1-3} alkylene"), or 1 to 2 carbon atoms ("C_{1-2} alkylene").

"Cycloalkyl" refers to a fully or partially saturated hydrocarbon ring system that has the specified number of carbon atoms, which may be a monocyclic, bridged or fused bicyclic, or polycyclic ring system that is connected to the base molecule through a carbon atom of the

cycloalkyl ring. "Cycloalkyl" can refer to the ring system being a fully saturated hydrocarbon ring system. Cycloalkyl groups may contain, but are not limited to, 3 to 12 carbon atoms ("C_{3-12} cycloalkyl"), 3 to 8 carbon atoms ("C_{3-8} cycloalkyl"), 3 to 6 carbon atoms ("C_{3-6} cycloalkyl"), 3 to 5 carbon atoms ("C_{3-5} cycloalkyl") or 3 to 4 carbon atoms ("C_{3-4} cycloalkyl"). Examples include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantanyl, and the like. Cycloalkyl groups may be optionally substituted, unsubstituted or substituted, as further defined herein.

"Heterocycloalkyl" refers to a fully or partially saturated ring system containing the specified number of ring atoms and containing at least one heteroatom selected from N, O, and S as a ring member, where ring S atoms are optionally substituted by one or two oxo groups (i.e., $S(=O)_q$, where q is 0, 1 or 2) and where the heterocycloalkyl ring is connected to the base molecule via a ring atom, which may be C or N. The heterocycloalkyl can refer to the ring system being fully saturated. Heterocycloalkyl rings include rings which are spirocyclic, bridged, or fused to one or more other heterocycloalkyl or carbocyclic rings, where such spirocyclic, bridged, or fused rings may themselves be saturated, partially unsaturated, or aromatic to the extent unsaturation or aromaticity makes chemical sense, provided the point of attachment to the base molecule is an atom of the heterocycloalkyl portion of the ring system. Heterocycloalkyl rings may contain 1 to 4 heteroatoms selected from N, O, and $S(=O)_q$ as ring members, or 1 to 2 ring heteroatoms, provided that such heterocycloalkyl rings do not contain two contiguous oxygen or sulfur atoms.

Heterocycloalkyl rings may be optionally substituted or unsubstituted, as further defined herein. Such substituents may be present on the heterocyclic ring attached to the base molecule, or on a spirocyclic, bridged or fused ring attached thereto. Heterocycloalkyl rings may include, but are not limited to, 3-8 membered heterocyclyl groups, for example 4-7 or 4-6 membered heterocycloalkyl groups, in accordance with the definition herein.

"Aryl" or "aromatic" refers to monocyclic, bicyclic (e.g., biaryl, fused), or polycyclic ring systems that contain the specified number of ring atoms, in which all carbon atoms in the ring are of sp^2 hybridization and in which the pi electrons are in conjugation. Aryl groups may contain, but are not limited to, 6 to 20 carbon atoms ("C_{6-20} aryl"), 6 to 14 carbon atoms ("C_{6-14} aryl"), 6 to 12 carbon atoms ("C_{6-12} aryl"), or 6 to 10 carbon atoms ("C_{6-10} aryl"). Fused aryl groups may include an aryl ring (e.g., a phenyl ring) fused to another aryl ring. Examples include, but are not limited to, phenyl, biphenyl, naphthyl, anthracenyl, phenanthrenyl, indanyl, and indenyl. Aryl groups may be optionally substituted, unsubstituted or substituted, as further defined herein.

Similarly, "heteroaryl" or "heteroaromatic" refer to monocyclic, bicyclic (e.g., heterobiaryl, fused), or polycyclic ring systems that contain the specified number of ring atoms and include at least one heteroatom selected from N, O, and S as a ring member in a ring in which all carbon atoms in the ring are of sp^2 hybridization and in which the pi electrons are in conjugation.

Heteroaryl groups may contain, but are not limited to, 5 to 20 ring atoms ("5-20 membered heteroaryl"), 5 to 14 ring atoms ("5-14 membered heteroaryl"), 5 to 12 ring atoms ("5-12 membered heteroaryl"), 5 to 10 ring atoms ("5-10 membered heteroaryl"), 5 to 9 ring atoms ("5-9 membered heteroaryl"), or 5 to 6 ring atoms ("5-6 membered heteroaryl"). Heteroaryl rings are attached to the base molecule via a ring atom of the heteroaromatic ring. Thus, either 5- or 6-membered heteroaryl rings, alone or in a fused structure, may be attached to the base molecule via a ring C or N atom. Examples of heteroaryl groups include, but are not limited to, pyrrolyl, furanyl, thiophenyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridinyl, pyridizinyl, pyrimidinyl, pyrazinyl, benzofuranyl, benzothiophenyl, indolyl, benzimidazolyl, indazolyl, quinolinyl, isoquinolinyl, purinyl, triazinyl, naphthyridinyl, cinnolinyl, quinazolinyl, quinoxalinyl and carbazolyl. Examples of 5- or 6-membered heteroaryl groups include, but are not limited to, pyrrolyl, furanyl, thiophenyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, triazolyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl rings. Heteroaryl groups may be optionally substituted, unsubstituted or substituted, as further defined herein.

"Heterocycle" or "heterocyclic" refers to a cyclic ring system that includes at least one heteroatom selected from N, O, and S as a ring member in the ring system. The ring system can include heterocycloalkyl or heteroaryl rings. The ring system can include spirocyclic rings, bridged rings, or fused rings.

"Amino" refers to a group $-NH_2$, which is unsubstituted or substituted. When substituted, the term includes groups of the form $-NR_xR_y$, one of R_x and R_y is an alkyl moiety and the other is H, or both of R_x and R_y are alkyl moieties, where the alkyl moieties have the specified number of carbon atoms (e.g., $-NH(C_{1-3}$ alkyl) or $-N(C_{1-3}$ alkyl$)_2$). The term "aminoheterocycloalkyl" refers to a heterocycloalkyl substituted with an amino group.

The term "pharmaceutically acceptable" means the substance (e.g., the compounds described herein) and any salt thereof, or composition containing the substance or salt of the compounds of the disclosure is suitable for administration to a subject or patient.

A "pharmaceutical composition" refers to a mixture of one or more of the compounds of the disclosure, or a pharmaceutically acceptable salt, solvate, hydrate or prodrug thereof as an active ingredient, and at least one pharmaceutically acceptable excipient.

"Deuterium enrichment factor" as used herein means the ratio between the deuterium abundance and the natural abundance of deuterium, each relative to hydrogen abundance. An atomic position designated as having deuterium typically can have a deuterium enrichment factor of, at least 1,000 (15% deuterium incorporation), at least 2,000 (30% deuterium incorporation), at least 3,000 (45% deuterium incorporation), at least 3,500 (52.5% deuterium incorporation), at least 3,500 (52.5% deuterium incorporation at each designated deuterium atom), at least 4,000 (60% deuterium incorporation), at least 4,500 (67.5% deuterium incorporation), at least 5,000 (75% deuterium incorporation), at least 5,500 (82.5% deuterium

incorporation), at least 6,000 (90% deuterium incorporation), at least 6,333.3 (95% deuterium incorporation), at least 6,466.7 (97% deuterium incorporation), at least 6,600 (99% deuterium incorporation), or at least 6,633.3 (99.5% deuterium incorporation).

"Excipient" as used herein describes any ingredient other than the compound(s) of the disclosure. The choice of excipient will to a large extent depend on factors such as the mode of administration, the effect of the excipient on solubility and stability, and the nature of the dosage form. As used herein, "excipient" includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, carriers, diluents and the like that are physiologically compatible. Examples of excipients include one or more of water, saline, phosphate buffered saline, dextrose, glycerol, ethanol and the like, as well as combinations thereof, and may include isotonic agents, for example, sugar, sodium chloride, or polyalcohol such as mannitol, or sorbitol in the composition. Examples of excipients also include various organic solvents (such as hydrates and solvates). The pharmaceutical compositions may, if desired, contain additional excipients such as flavorings, binders/binding agents, lubricating agents, disintegrants, sweetening or flavoring agents, coloring matters or dyes, and the like. For example, for oral administration, tablets containing various excipients, such as citric acid may be employed together with various disintegrants such as starch, alginic acid and certain complex silicates and with binding agents such as sucrose, gelatin and acacia. Examples, without limitation, of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils and polyethylene glycols. Additionally, lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc are often useful for tableting purposes. Solid compositions of a similar type may also be employed in soft and hard filled gelatin capsules. Non-limiting examples of excipients, therefore, also include lactose or milk sugar and high molecular weight polyethylene glycols. When aqueous suspensions or elixirs are desired for oral administration the active compound therein may be combined with various sweetening or flavoring agents, coloring matters or dyes and, if desired, emulsifying agents or suspending agents, together with additional excipients such as water, ethanol, propylene glycol, glycerin, or combinations thereof. Examples of excipients also include pharmaceutically acceptable substances such as wetting agents or minor amounts of auxiliary substances such as wetting or emulsifying agents, preservatives, or buffers, which enhance the shelf life or effectiveness of the compound.

The term "treating", "treat", or "treatment" as used herein embraces both preventative, i.e., prophylactic, and palliative treatment, i.e., relieve, alleviate, or slow the progression of the patient's disease (or condition) or any tissue damage associated with the disease.

As used herein, the term, "subject", "individual", or "patient," used interchangeably, refers to any animal, including mammals. Mammals according to the disclosure include canine, feline, bovine, caprine, equine, ovine, porcine, rodents, lagomorphs, primates, humans, and the

like, and encompass mammals in utero. Humans can be suitable subjects. Human subjects may be of any gender and at any stage of development.

As used herein, the phrase "therapeutically effective amount" refers to the amount of active compound or pharmaceutical agent 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, which may include one or more of the following:

(1) preventing the disease; for example, preventing a disease, condition, or disorder in an individual that may be predisposed to the disease, condition, or disorder but does not yet experience or display the pathology or symptomatology of the disease;

(2) inhibiting the disease; for example, inhibiting a disease, condition, or disorder in an individual that is experiencing or displaying the pathology or symptomatology of the disease, condition, or disorder (i.e., arresting (or slowing) further development of the pathology or symptomatology or both); and

(3) ameliorating the disease; for example, ameliorating a disease, condition, or disorder in an individual that is experiencing or displaying the pathology or symptomatology of the disease, condition, or disorder (i.e., reversing the pathology or symptomatology or both).

Salts encompassed within the term "pharmaceutically acceptable salts" refer to the compounds of this disclosure, which are generally prepared by reacting the free base or free acid with a suitable organic or inorganic acid, or a suitable organic or inorganic base, respectively, to provide a salt of the compound of the disclosure that is suitable for administration to a subject or patient.

In addition, the compound of the disclosure may also include other salts of such compounds which are not necessarily pharmaceutically acceptable salts, which may be useful as intermediates for one or more of the following: 1) preparing a compound of the disclosure; 2) purifying the compound of the disclosure; 3) separating enantiomers of the compound of the disclosure; or 4) separating diastereomers of the compound of the disclosure.

Suitable acid addition salts are formed from acids which form non-toxic salts. Examples include, but are not limited to, acetate, adipate, aspartate, benzoate, besylate, bicarbonate/carbonate, bisulfate/sulfate, borate, camsylate, citrate, cyclamate, edisylate, esylate, formate, fumarate, gluceptate, gluconate, glucuronate, hexafluorophosphate, hibenzate, hydrochloride/chloride, hydrobromide/bromide, hydroiodide/iodide, isethionate, lactate, malate, maleate, malonate, mesylate, methylsulfate, naphthylate, 2-napsylate, nicotinate, nitrate, orotate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, pyroglutamate, saccharate, stearate, succinate, tannate, tartrate, tosylate, trifluoroacetate, 1,5-naphathalenedisulfonic acid and xinofoate salts. The salt can be a trifluoroacetate salt or a formate salt.

Suitable base salts are formed from bases which form non-toxic salts. Examples include, but are not limited to aluminum, arginine, benzathine, calcium, choline, diethylamine,

diolamine, glycine, lysine, magnesium, meglumine, olamine, potassium, sodium, tromethamine and zinc salts.

Hemisalts of acids and bases may also be formed, for example, hemisulfate and hemicalcium salts.

For a review on suitable salts, see Paulekun, G. S. et al., Trends in Active Pharmaceutical Ingredient Salt Selection Based on Analysis of the Orange Book Database, J. Med. Chem. 2007; 50(26), 6665-6672.

Pharmaceutically acceptable salts of the compounds of the disclosure may be prepared by methods well known to one skilled in the art, including but not limited to the following procedures

(i) by reacting a compound of the disclosure with the desired acid or base;

(ii) by removing an acid- or base-labile protecting group from a suitable precursor of a compound of the disclosure or by ring-opening a suitable cyclic precursor, for example, a lactone or lactam, using the desired acid or base; or

(iii) by converting one salt of a compound of the disclosure to another. This may be accomplished by reaction with an appropriate acid or base or by means of a suitable ion exchange procedure.

These procedures are typically carried out in solution. The resulting salt may precipitate out and be collected by filtration or may be recovered by evaporation of the solvent.

The compounds of the disclosure, and pharmaceutically acceptable salts thereof, may exist in unsolvated and solvated forms. The term 'solvate' is used herein to describe a molecular complex comprising the compound of the disclosure, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is employed when said solvent is water.

In addition, the compounds of the disclosure may also include other solvates of such compounds which are not necessarily pharmaceutically acceptable solvates, which may be useful as intermediates for one or more of the following: 1) preparing the compounds of the disclosure; 2) purifying the compounds of the disclosure; 3) separating enantiomers of the compounds of the disclosure; or 4) separating diastereomers of the compounds of the disclosure.

A currently accepted classification system for organic hydrates is one that defines isolated site, channel, or metal-ion coordinated hydrates - see Polymorphism in Pharmaceutical Solids by K. R. Morris (Ed. H. G. Brittain, Marcel Dekker, 1995). Isolated site hydrates are ones in which the water molecules are isolated from direct contact with each other by intervening organic molecules. In channel hydrates, the water molecules lie in lattice channels where they are next to other water molecules. In metal-ion coordinated hydrates, the water molecules are bonded to the metal ion.

When the solvent or water is tightly bound, the complex may have a well-defined stoichiometry independent of humidity. When, however, the solvent or water is weakly bound, as in channel solvates and hygroscopic compounds, the water/solvent content may be dependent on humidity and drying conditions. In such cases, non-stoichiometry will be the norm.

Also included within the scope of the disclosure are multi-component complexes (other than salts and solvates) wherein the drug and at least one other component are present in stoichiometric or non-stoichiometric amounts. Complexes of this type include clathrates (drug-host inclusion complexes) and co-crystals. The latter are typically defined as crystalline complexes of neutral molecular constituents which are bound together through non-covalent interactions, for example, hydrogen bonded complex (cocrystal) may be formed with either a neutral molecule or with a salt. Co-crystals may be prepared by melt crystallization, by recrystallization from solvents, or by physically grinding the components together - see Chem Commun, 17;1889-1896, by O. Almarsson and M. J. Zaworotko (2004). For a general review of multi-component complexes, see J Pharm Sci, 64(8), 1269-1288, by Haleblian (August 1975).

The compounds of the disclosure may exist in a continuum of solid states ranging from amorphous to crystalline. The term 'amorphous' refers to a state in which the material lacks long range order at the molecular level and, depending upon temperature, may exhibit the physical properties of a solid or a liquid. Typically, such materials do not give distinctive X-ray diffraction patterns and, while exhibiting the properties of a solid, are more formally described as a liquid. Upon heating, a change from solid to liquid properties occurs which is characterized by a change of state, typically second order ('glass transition'). The term 'crystalline' refers to a solid phase in which the material has a regular ordered internal structure at the molecular level and gives a distinctive X-ray diffraction pattern with defined peaks. Such materials when heated sufficiently will also exhibit the properties of a liquid, but the change from solid to liquid is characterized by a phase change, typically first order ('melting point').

The compounds of the disclosure may also exist in a mesomorphic state (mesophase or liquid crystal) when subjected to suitable conditions. The mesomorphic state is intermediate between the true crystalline state and the true liquid state (either melt or solution) and consists of two dimensional order on the molecular level. Mesomorphism arising as the result of a change in temperature is described as 'thermotropic' and that resulting from the addition of a second component, such as water or another solvent, is described as 'lyotropic'. Compounds that have the potential to form lyotropic mesophases are described as 'amphiphilic' and consist of molecules which possess an ionic (such as $-COO^-Na^+$, $-COO^-K^+$, or $-SO_3^-Na^+$) or non-ionic (such as $-N^+N^+(CH_3)_3$) polar head group. For more information, see Crystals and the Polarizing Microscope by N. H. Hartshorne and A. Stuart, 4th Edition (Edward Arnold, 1970).

Compounds of the disclosure may exist as two or more stereoisomers. Stereoisomers of the compounds may include *cis* and *trans* isomers (geometric isomers), optical isomers such as

R and *S* enantiomers, diastereomers, rotational isomers, atropisomers, and conformational isomers. For example, compounds of the disclosure containing one or more asymmetric carbon atoms may exist as two or more stereoisomers. Where a compound of the disclosure contains an alkenyl or alkenylene group, geometric cis/trans (or Z/E) isomers are possible. Cis/trans isomers may also exist for saturated rings.

The pharmaceutically acceptable salts of the compounds of the disclosure may also contain a counterion which is optically active (e.g., d-lactate or l-lysine) or racemic (e.g., dl-tartrate or dl-arginine).

Cis/trans isomers may be separated by conventional techniques well known to those skilled in the art, for example, chromatography and fractional crystallization.

Conventional techniques for the preparation/isolation of individual enantiomers include chiral synthesis from a suitable optically pure precursor or resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high pressure liquid chromatography (HPLC). Alternatively, the racemate (or a racemic precursor) may be reacted with a suitable optically active compound, for example, an alcohol, or, in the case where a compound of the disclosure contains an acidic or basic moiety, a base or acid such as 1-phenylethylamine or tartaric acid. The resulting diastereomeric mixture may be separated by chromatography, fractional crystallization, or by using both of said techniques, and one or both of the diastereoisomers converted to the corresponding pure enantiomer(s) by means well known to a skilled person. Chiral compounds of the disclosure (and chiral precursors thereof) may be obtained in enantiomerically-enriched form using chromatography, typically HPLC Concentration of the eluate affords the enriched mixture. Chiral chromatography using sub-and supercritical fluids may be employed. Methods for chiral chromatography useful in the present disclosure are known in the art (see, for example, Smith, Roger M., Loughborough University, Loughborough, UK; Chromatographic Science Series (1998), 75 (Supercritical Fluid Chromatography with Packed Columns), pp. 223-249 and references cited therein).

When any racemate crystallizes, crystals of two different types are possible. The first type is the racemic compound (true racemate) referred to above wherein one homogeneous form of crystal is produced containing both enantiomers in equimolar amounts. The second type is the racemic mixture or conglomerate wherein two crystal forms are produced in equimolar amounts each comprising a single enantiomer. While both of the crystal forms present in a racemic mixture have identical physical properties, they may have different physical properties compared to the true racemate. Racemic mixtures may be separated by conventional techniques known to those skilled in the art - see, for example, Stereochemistry of Organic Compounds by E. L. Eliel and S. H. Wilen (Wiley, 1994).

Where structural isomers are interconvertible via a low energy barrier, tautomeric isomerism ('tautomerism') may occur. This may take the form of proton tautomerism in the compounds of the disclosure containing, for example, an imino/amino, keto/enol, or

oxime/nitroso group, lactam/lactim or so-called valence tautomerism in compounds which contain an aromatic moiety. It follows that a single compound may exhibit more than one type of isomerism.

It must be emphasized that while, for conciseness, the compounds of the disclosure have been drawn herein in a single tautomeric form, all possible tautomeric forms are included within the scope of the disclosure.

The present disclosure includes all pharmaceutically acceptable isotopically-labeled compounds of Formula I wherein one or more atoms are replaced by atoms having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number which predominates in nature.

Examples of isotopes suitable for inclusion in the compounds of Formula I may include isotopes of hydrogen, such as ^{2}H (D, deuterium) and ^{3}H (T, tritium), carbon, such as ^{11}C, ^{13}C and ^{14}C, chlorine, such as ^{36}Cl, fluorine, such as ^{18}F, iodine, such as ^{123}I and ^{125}I, nitrogen, such as ^{13}N and ^{15}N, oxygen, such as ^{15}O, ^{17}O and ^{18}O, phosphorus, such as ^{32}P, and sulfur, such as ^{35}S.

Certain isotopically-labelled compounds of Formula I, for example, those incorporating a radioactive isotope, are useful in one or both of drug or substrate tissue distribution studies. The radioactive isotopes, such as, tritium and ^{14}C are particularly useful for this purpose in view of their ease of incorporation and ready means of detection. Substitution with positron emitting isotopes, such as, ^{11}C, ^{18}F, ^{15}O and ^{13}N, may be useful in Positron Emission Topography (PET) studies for examining substrate receptor occupancy. Substitution with deuterium, i.e., ^{2}H, may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased in vivo half-life, reduced dosage requirements, reduced CYP450 inhibition (competitive or time dependent), or an improvement in therapeutic index or tolerability.

The disclosure provides deuterium-labeled (or deuterated) compounds and salts, where the formula and variables of such compounds and salts are each and independently as described herein. "Deuterated" means that at least one of the atoms in the compound is deuterium in an abundance that is greater than the natural abundance of deuterium (typically approximately 0.015%). A skilled artisan recognized that in chemical compounds with a hydrogen atom, the hydrogen atom actually represents a mixture of H and D, with about 0.015% being D. The concentration of the deuterium incorporated into the deuterium-labeled compounds and salt of Formula I may be defined by the deuterium enrichment factor. It is understood that one or more deuterium may exchange with hydrogen under physiological conditions.

The deuterium compound can be selected from any one of the compounds of the examples specifically illustrated in the Examples section.

One or more hydrogen atoms on certain metabolic sites on the compounds of Formula I can be deuterated.

Isotopically-labeled compounds of Formula I may generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Preparations using an appropriate isotopically-labeled reagent in place of the non-labeled reagent previously employed.

Pharmaceutically acceptable solvates in accordance with the disclosure include those wherein the solvent of crystallization may be isotopically substituted, e.g., D_2O, d_6-acetone, d_6-DMSO.

A compound of the disclosure may be administered in the form of a prodrug. Thus, certain derivatives of a compound of the disclosure which may have little or no pharmacological activity themselves may, when administered into or onto the body, be converted into a compound of the disclosure having the desired activity, for example by hydrolytic cleavage, particularly hydrolytic cleavage promoted by an esterase or peptidase enzyme. Such derivatives are referred to as 'prodrugs'. Further information on the use of prodrugs may be found in 'The Expanding Role of Prodrugs in Contemporary Drug Design and Development, Nature Reviews Drug Discovery, 17, 559-587 (2018) (J. Rautio et al.).

Prodrugs in accordance with the disclosure may, for example, be produced by replacing appropriate functionalities present in the compounds of the disclosure with certain moieties known to those skilled in the art as 'pro-moieties' as described, for example, in 'Design of Prodrugs' by H. Bundgaard (Elsevier, 1985).

Thus, a prodrug in accordance with the disclosure may be (a) an ester or amide derivative of a carboxylic acid when present in a compound of the disclosure; (b) an ester, carbonate, carbamate, phosphate or ether derivative of a hydroxyl group when present in a compound of the disclosure; (c) an amide, imine, carbamate or amine derivative of an amino group when present in a compound of the disclosure; (d) a thioester, thiocarbonate, thiocarbamate or sulfide derivatives of a thiol group when present in a compound of the disclosure; or (e) an oxime or imine derivative of a carbonyl group when present in a compound of the disclosure.

Some specific examples of prodrugs in accordance with the disclosure include:

(i) when a compound of the disclosure contains a carboxylic acid functionality (-COOH), an ester thereof, such as a compound wherein the hydrogen of the carboxylic acid functionality of the compound is replaced by C_{1-8} alkyl (e.g., ethyl) or (-C_{1-8} alkyl)C(=O)OCH_2- (e.g., ^{t}BuC(=O)OCH_2-);

(ii) when a compound of the disclosure contains an alcohol functionality (-OH), an ester thereof, such as a compound wherein the hydrogen of the alcohol functionality of the compound is replaced by –CO(C_{1-8} alkyl) (e.g., methylcarbonyl) or the alcohol is esterified with an amino acid;

(iii) when a compound of the disclosure contains an alcohol functionality (-OH), an ether thereof, such as a compound wherein the hydrogen of the alcohol functionality of the compound is replaced by (C_{1-8} alkyl)C(=O)OCH_2- or $–CH_2OP(=O)(OH)_2$;

(iv) when a compound of the disclosure contains an alcohol functionality (-OH), a phosphate thereof, such as a compound wherein the hydrogen of the alcohol functionality of the compound is replaced by $–P(=O)(OH)_2$ or $–P(=O)(O^-Na^+)_2$ or $–P(=O)(O^-)_2Ca^{2+}$;

(v) when a compound of the disclosure contains a primary or secondary amino functionality (-NH_2 or -NHR where R ≠ H), an amide thereof, for example, a compound wherein, as the case may be, one or both hydrogens of the amino functionality of the compound is/are replaced by (C_{1-10})alkanoyl, $–COCH_2NH_2$ or the amino group is derivatized with an amino acid;

(vi) when a compound of the disclosure contains a primary or secondary amino functionality (-NH_2 or -NHR where R ≠ H), an amine thereof, for example, a compound wherein, as the case may be, one or both hydrogens of the amino functionality of the compound is/are replaced by $–CH_2OP(=O)(OH)_2$.

Certain compounds of the disclosure may themselves act as prodrugs of other compounds the disclosure it is also possible for two compounds of the disclosure to be joined together in the form of a prodrug. In certain circumstances, a prodrug of a compound of the disclosure may be created by internally linking two functional groups in a compound of the disclosure, for instance by forming a lactone.

Also included within the scope of the disclosure are active metabolites of compounds of the disclosure, that is, compounds formed in vivo upon administration of the drug, often by oxidation or dealkylation. Some examples of metabolites in accordance with the disclosure include, but are not limited to,

(i) where the compound of the disclosure contains an alkyl group, a hydroxyalkyl derivative thereof (-CH → -COH):

(ii) where the compound of the disclosure contains an alkoxy group, a hydroxy derivative thereof (-OR → -OH);

(iii) where the compound of the disclosure contains a tertiary amino group, a secondary amino derivative thereof (-NRR' → -NHR or –NHR');

(iv) where the compound of the disclosure contains a secondary amino group, a primary derivative thereof (-NHR → -NH_2);

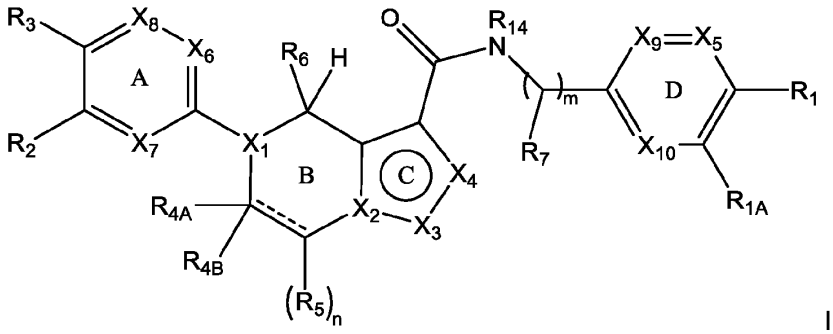
(v) where the compound of the disclosure contains a phenyl moiety, a phenol derivative thereof (-Ph → -PhOH);

(vi) where the compound of the disclosure contains an amide group, a carboxylic acid derivative thereof (-$CONH_2$ → COOH); and

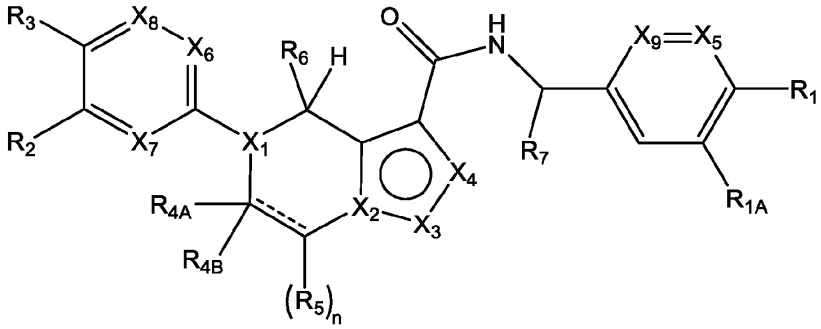
(vii) where the compound contains a hydroxy or carboxylic acid group, the compound may be metabolized by conjugation, for example, with glucuronic acid to form a glucuronide. Other routes of conjugative metabolism exist. These pathways are frequently known as Phase 2

metabolism and include, for example, sulfation or acetylation. Other functional groups, such as NH groups, may also be subject to conjugation.

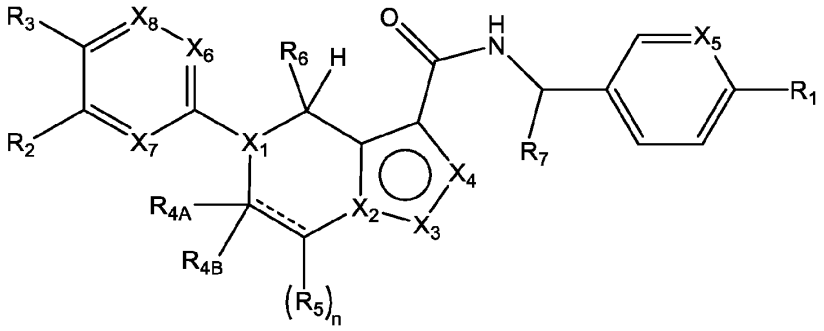
The compound or a pharmaceutically acceptable salt thereof can have the structure of Formula I or Formula IA or Formula IB. The compound of Formula I can have the structure of Formula IA or Formula IB.



I



IA



IB

X_1 can be CH, CNH_2, or N. X_1 can be N.

X_2 can be C or N.

X_3 can be CR_{13}, N, NR_{13}, O, or S. X_3 can be CR_{13}. X_3 can be N or NR_{13}. X_3 can be CR_{13} or N.

X_4 can be CH, N, or NR_{13}. X_4 can be CH, N, or N-cyclopropyl. X_4 can be N.

X_5 can be CH, CR_{1B}, or N. X_5 can be CH.

X_6 can be CH or N.

X_7 can be CH, N, or CF. X_7 can be CH or N. X_7 can be CCl.

X_8 can be CH or N. X_8 can be CH.

X_9 can be CH, CR_{1B}, or N.

X_{10} can be CH, CR_{1B}, or N. At least one of X_2 can be N or X_3 can be N, NH, or NR_{13}, and X_4 can be N.

If X_3 is S or O, then X_2 can be C.

If X_3 is CR_{13} or NR_{13}, then X_4 can be CH or N. If X_4 is NR_{13}, then X_3 can be N, O, or S.

The dashed line refers to the bond being a single bond (i.e., the dashed line is not present leaving only the single bond) or a double bond (i.e., the dashed line is present as a second bond making the double bond). The dashed line can refer to the bond being a single bond. If the dashed line refers to the bond being a double bond, then R_{4B} is absent and n is 1.

R_1 can be $-NHR_8$, -OH, $-C_{2-5}$ heterocycle, or $-C_{1-3}$ alkyl. R_1 can be $-NHR_8$, $-C_{2-5}$ heterocycle, or $-C_{1-3}$ alkyl. R_1 can be $-C_{2-5}$ heterocycle and can optionally be substituted with one or more or one, two, or three of $-C_{1-3}$ alkyl, $-C_{1-3}$ oxoalkyl, $-C_{3-5}$ heterocycloalkyl, $-C_{3-5}$ hydroxyheterocycloalkyl, $-C_{3-5}$ aminoheterocycloalkyl, or oxo. R_1 can be $-C_{2-5}$ heterocycle and can optionally be substituted with one or more or one, two, or three of $-C_{1-3}$ alkyl or oxo. R_1 can be $-C_{2-5}$ heterocycle and can optionally be substituted with oxo. R_1 can be $-C_{1-3}$ alkyl and can be substituted with one, two, or three of oxo, $-NR_{10A}R_{11}$, or $-NR_{10}R_{11}$. R_1 can be $-C_{1-3}$ alkyl and can be substituted with one or two of oxo, $-NR_{10A}R_{11}$, or $-NR_{10}R_{11}$. R_1 can be $-C_{1-3}$ alkyl optionally substituted with one or more or one, two, or three of oxo or $-NR_{10}R_{11}$. R_1 can be $-C_{1-3}$ alkyl substituted with oxo and $-NR_{10}R_{11}$. R_1 can be $-C_{1-3}$ alkyl substituted with oxo and $-NR_{10A}R_{11}$. R_1 can be $-NHR_8$. Each of the $-C_{2-5}$ heterocycle, $-C_{3-5}$ heterocycloalkyl, $-C_{3-5}$ hydroxyheterocycloalkyl, and the $-C_{3-5}$ aminoheterocycloalkyl independently can include 1 to 4 heteroatoms including at least one of N, O, or S. The $-C_{2-5}$ heterocycle of R_1 can include 1 to 4 heteroatoms including at least one of N, O, or S; where the heteroatoms can all be N.

R_{1A} can be H. R_{1A} can be $-CH_3$. R_{1A} can be H, halogen, or $-CH_3$. R_{1A} can be H or halogen, where the halogen can be F.

R_1 and R_{1A} can form a C_{5-7} heterocycloalkyl fused to Ring D or a C_{5-7} heteroaryl fused to Ring D. The C_{5-7} heterocycloalkyl or the C_{5-7} heteroaryl can optionally be substituted with oxo. R_1 and R_{1A} can form a C_{6-8} fused heterocycloalkyl that is optionally substituted with oxo. R_1 and R_{1A} can form a C_{6-8} fused heteroaryl that is optionally substituted with oxo. Each of the C_{6-8} fused heterocycloalkyl and the can C_{6-8} fused heteroaryl independently can include 1 to 3 heteroatoms including at least one of N, O, or S.

Each R_{1B} independently is H, $-CH_3$, F, Cl, or methoxy.

R_2 can be H, $-C_{1-3}$ alkyl, $-C_{1-3}$ alkoxy, $-C_{1-3}$ fluoroalkyl, or halogen. R_2 can be H.

R_3 can be $-C_{1-3}$ alkyl, $-C_{2-10}$ heterocycle, $-P(=O)(CH_3)_2$, $-S(=O)CH_3$, $-NH-S(=O)_2CH_3$, or $-NH-C(=O)-C_{1-3}$ alkyl. R_3 can be $-C_{1-3}$ alkyl, $-C_{2-10}$ heterocycle, $-P(=O)(CH_3)_2$, $-S(=O)CH_3$, or $-NH-S(=O)_2CH_3$. R_3 can be $-C_{1-3}$ alkyl, $-C_{2-10}$ heterocycle, or $-NH-C(=O)-C_{1-3}$ alkyl. R_3 can be $-C_{1-3}$ alkyl optionally substituted with one or more or one, two, or three of oxo, -OH, halogen, $-C_{3-}$

$_6$ cycloalkyl, -$NR_{12}R_{12A}$, -C_{5-8} heterocycle, or cyano. R_3 can be -C_{1-3} alkyl substituted with oxo and -$NR_{12}R_{12A}$. The -C_{2-10} heterocycle of R_3 can be -C_{2-10} heterocycloalkyl or -C_{2-10} heteroaryl. The -C_{2-10} heterocycle of R_3 can be -C_{2-6} heterocycloalkyl or -C_{2-6} heteroaryl. R_3 can be -C_{2-10} heterocycle optionally substituted with one or more or one, two, or three of -OH, halogen, -C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy, -C_{1-3} alkyl, -C_{1-3} fluoroalkyl, cyclopropyl, or oxo. R_3 can be -C_{2-10} heterocycloalkyl optionally substituted with one or more or one, two, or three of -OH, halogen, -C_{1-3} hydroxyalkyl, -C_{1-3} alkyl, cyclopropyl, or oxo. R_3 can be -C_{1-3} alkyl optionally substituted with one or more or one, two, or three of oxo or -$NR_{12}R_{12A}$. R_3 can be -C_{2-5} heterocycle optionally substituted with -C_{1-3} alkyl. R_3 can be -C_{2-5} heteroaryl optionally substituted with one or more or one, two, or three -C_{1-3} alkyl. Each of the -C_{2-10} heterocycle, -C_{5-8} heterocycle, -C_{2-6} heterocycloalkyl, -C_{2-10} heterocycloalkyl, -C_{2-10} heteroaryl, -C_{2-6} heteroaryl, or -C_{2-5} heterocycle independently can include 1 to 3 heteroatoms including at least one of N, O, or S. The -C_{2-10} heterocycle of R_3 can include 1 to 3 heteroatoms including at least one of N, O, or S. The -C_{2-10} heterocycle of R_3 can be a spiro, fused, or bridged -C_{2-10} heterocycle. The C_{5-8} heterocycle of R_3 can include 1 to 4 heteroatoms including at least one of N, O, or S.

R_2 and R_3 can form a C_{3-6} heterocycle fused to Ring A optionally substituted with one, two, or three of -C_{1-3} alkyl, -C_{2-3} oxoalkyl, or oxo. R_2 and R_3 can form a C_{3-6} heterocycloalkyl fused to Ring A optionally substituted with one or more or one, two, or three of -C_{1-3} alkyl, -C_{2-3} oxoalkyl, or oxo. Each of the C_{3-6} heterocycle or the C_{3-6} heterocycloalkyl independently can include 1 to 3 heteroatoms including at least one of N, O, or S.

R_{4A} can be H, -OH, -C_{1-3} fluoroalkyl, or -C_{1-3} alkyl. R_{4A} can be H, -C_{1-3} fluoroalkyl, or -C_{1-3} alkyl.

R_{4B} can be H. R_{4B} can be absent.

R_{4A} and R_{4B} taken together can form cyclopropyl.

R_{4B} and one R_5 taken together can form a C_{3-5} cycloalkyl fused to Ring B.

Each R_5 independently can be H, -OH, -C_{3-6} cycloalkyl (e.g., cyclopropyl), halogen, -C_{1-3} fluoroalkyl, or -C_{1-3} alkyl. Each R_5 independently can be H, halogen, or -C_{1-3} alkyl. The two R_5 groups taken together can form cyclopropyl. If the dashed line represents a double bond being present, then R_5 can be H, -C_{3-6} cycloalkyl (e.g., cyclopropyl), halogen, -C_{1-3} fluoroalkyl, or -C_{1-3} alkyl.

R_6 can be H, -OH, or -C_{1-3} alkyl. R_6 can be H or -C_{1-3} alkyl.

R_{4A} and R_6 taken together can form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge. One R_5 and R_6 taken together can form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge. The C_{1-3} heteroalkyl bridge can include one heteroatom of N, O, or S.

R_7 can be H, -C_{1-3} alkyl, or -C_{1-3} hydroxyalkyl. R_7 can be H or -C_{1-3} alkyl.

R_8 can be H, -C_{1-3} alkyl, -SO_2CH_3, or a -C_{3-4} heterocycle. R_8 can be H, -C_{1-3} alkyl, or a -C_{3-4} heterocycle. R_8 can be -C_{1-3} alkyl substituted with one, two, or three of oxo, -C_{3-9} heterocycloalkyl, -C_{3-9} heterocycloalkyl substituted with methyl, -C_{1-3} alkoxy, cyanoimine,

or -NR_9R_{10}. R_8 can be -C_{1-3} alkyl optionally substituted with one or more or one, two, or three of oxo or -NR_9R_{10}. R_8 can be -C_{1-3} alkyl optionally substituted with one or two of oxo or -NR_9R_{10}. R_8 can be -C_{1-3} alkyl substituted with oxo and -NR_9R_{10}. R_8 can be -C_{3-4} heterocycle optionally substituted with one, two, or three of oxo, halogen, -C_{0-1} alkylene-$NR_{10}R_{11}$, -OH, -C_{1-3} hydroxyalkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, -C_{1-3} oxoalkyl, -C_{1-3} alkyl, or -C_{1-3} alkoxy optionally substituted with -$NR_{10}R_{11}$. The -C_{3-9} heterocycloalkyl of R_8 can be substituted with one, two, or three of -C_{1-3} alkyl, -OH, -C_{1-3} hydroxyalkyl, -O-C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy, -C_{1-3} alkyl-C_{1-3} alkoxy, halogen, -C_{1-3} fluoroalkyl, -C_{1-3} fluoroalkoxy, cyano, -C_{1-3} cyanoalkyl, -C_{0-1} alkylene-C_{3-5} heterocycloalkyl, -O-C_{3-5} heterocycloalkyl, -C_{0-1} alkylene-$NR_{10}R_{11}$. R_8 can be -C_{3-4} heterocycle optionally substituted with one or more or one, two, or three of oxo or -C_{1-3} alkyl. Each of the -C_{3-4} heterocycle or the -C_{3-9} heterocycloalkyl of R_8 independently can include 1 to 4 heteroatoms including at least one of N, O, or S. The -C_{3-4} heterocycle of R_8 can include 1 to 4 heteroatoms including at least one of N or O. The -C_{3-9} heterocycloalkyl of R_8 can include 1 to 3 heteroatoms including at least one of N or O. The -C_{3-4} heterocycle or the -C_{3-9} heterocycloalkyl of R_8 can be a bridged, spiro, or fused heterocycle.

R_9 can be H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$, or -C_{3-5} heterocycloalkyl. R_9 can be the -C_{1-4} alkyl optionally substituted with one or more or one, two, or three of -C_{3-5} cycloalkyl, -C_{3-5} heterocycloalkyl, or methoxy. R_9 can be -C_{3-5} cycloalkyl of R_9 optionally substituted with one or two of -OH or -C_{1-3} alkyl. R_9 can be H or -C_{1-4} alkyl. Each of the -C_{3-5} heterocycloalkyl of R_9 independently can include 1 to 2 heteroatoms including at least one of N or O.

Each R_{10} independently can be H or -C_{1-4} alkyl. Each R_{10} independently can be H or -C_{1-3} alkyl.

R_{10A} can be -C_{0-1} alkylene-C_{3-5} heterocycloalkyl optionally substituted with -C_{1-3} alkyl. The C_{3-5} heterocycloalkyl of R_{10A} can include 1 heteroatom of N.

If the -C_{1-3} alkyl of R_8 is substituted with -NR_9R_{10}, then the corresponding R_9 and R_{10} can optionally be combined to form the C_{3-9} heterocycloalkyl or the C_{3-9} heterocycloalkyl.

Each R_{11} independently can be H or -C_{1-3} alkyl.

R_{12} can be H, -C_{1-3} alkyl, -C_{1-3} hydroxyalkyl, -$(CH_2)_{0-2}$-C_{3-5} heterocycloalkyl, -$(CH_2)_{1-2}$-O-C_{3-5} heterocycloalkyl, -methylene-C(=O)-$NR_{10}R_{11}$, or -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$. The -$(CH_2)_{0-2}$-C_{3-5} heterocycloalkyl or the -$(CH_2)_{1-2}$-O-C_{3-5} heterocycloalkyl of R_{12} can be substituted with -C_{1-4} alkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, -$(CH_2)_{0-1}$-phenyl, halogen, -C_{1-3} fluoroalkyl, or -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl. The -C_{1-3} alkyl of R_{12} can be substituted with one, two, or three of oxo or $NR_{10}R_{11}$. Each of the -$(CH_2)_{0-2}$-C_{3-5} heterocycloalkyl, the -$(CH_2)_{1-2}$-O-C_{3-5} heterocycloalkyl, or the -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl of R_{12} independently can include 1 to 2 heteroatoms including at least one of N or O.

R_{12A} can be H. R_{12A} can be -C_{1-4} alkyl.

R_{12} and R_{12A} can form a C_{3-10} heterocycle optionally substituted with one, two, or three of $-C_{1-3}$ alkyl, -OH, oxo, halogen, $-C_{2-3}$ oxoalkyl, $-C_{1-3}$ alkoxy, $-C_{1-3}$ hydroxyalkyl, $-C_{1-3}$ alkyl-C_{1-3} alkoxy, cyano, $-C_{3-6}$ cycloalkyl, $-S(=O)_2CH_3$, $-S(=O)_2CH_2CH_3$, $-C(=O)-NR_{10}R_{11}$, or $-NHC(=O)CH_3$. The C_{3-10} heterocycle can include 1 to 4 heteroatoms including at least one of N, O, or S. The C_{3-10} heterocycle can be a bridged, spiro, or fused heterocycle.

R_{13} can be H, $-C_{1-6}$ alkyl, $-C_{1-4}$ hydroxyalkyl, $-C_{1-3}$ fluoroalkyl, $-C_{1-3}$ alkyl-C_{1-3} alkoxy, $-C_{1-4}$ cyanoalkyl, $-C_{0-1}$ alkylene-C_{3-5} cycloalkyl, $-C_{2-4}$ oxoalkyl, or $-C_{0-1}$ alkylene-C_{3-5} heterocycloalkyl. R_{13} can be H, $-C_{1-4}$ alkyl, $-C_{1-4}$ hydroxyalkyl, $-C_{1-3}$ fluoroalkyl, $-C_{3-5}$ cycloalkyl, or $-C_{3-5}$ heterocycloalkyl. R_{13} can be H. R_{13} can be $-C_{0-1}$-cyclopropyl. The $-C_{1-6}$ alkyl of R_{13} can optionally be substituted with one, two, or three of oxo, fluoro, $-NH_2$, C_{3-6} cycloalkyl, or methoxy. The $-C_{3-5}$ cycloalkyl or the $-C_{3-6}$ cycloalkyl of R_{13} can optionally be substituted with one, two, or three of $-C_{1-3}$ alkyl, $-C_{1-3}$ fluoroalkyl, or halogen. The $-C_{3-5}$ heterocycloalkyl of R_{13} can include 1 to 3 heteroatoms including at least one of N, O, or S.

R_{14} can be H.

X_4 can be NR_{13} and R_{13} and R_{14} can form a C_{4-5} heterocycle fused to Ring C.

The variable n can be 1 or 2.

The variable m can be 0 or 1.

The respective heterocycles can each independently include 1 to 4 heteroatoms including at least one of N, O, or S.

At least one hydrogen of the compound of Formula I can be deuterium.

The A, B, C, and D values used to denote the rings in Formula I can be used to identify the corresponding rings of Formula IA and Formula IB.

The term "one or more of" when defining the number of groups in Formula I, IA, or IB can, for example, refer to one to four, or one to three of the listed options each time independently that the term is used.

The compound or a pharmaceutically acceptable salt thereof can be *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

The compound or a pharmaceutically acceptable salt thereof can be 5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

The compound or a pharmaceutically acceptable salt thereof can be 5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

The compound or a pharmaceutically acceptable salt thereof can be 5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

The compound or a pharmaceutically acceptable salt thereof can be (*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

The compound or a pharmaceutically acceptable salt thereof can be (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-N-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-c]pyridine-3-carboxamide.

The compound or a pharmaceutically acceptable salt thereof can be 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

A pharmaceutical composition can comprise a compound of Formula I. For example, the pharmaceutical composition can comprise a compound of Formula IA.

The compositions of the disclosure may be in a variety of forms. These include, for example, liquid, semi-solid and solid dosage forms, such as liquid solutions (e.g., injectable and infusible solutions), dispersions or suspensions, tablets, capsules, pills, powders, liposomes and suppositories. The form depends on the intended mode of administration and therapeutic application.

Typical compositions are in the form of injectable or infusible solutions, such as compositions similar to those used for passive immunization of humans with antibodies in general. One mode of administration is parenteral (e.g., intravenous, subcutaneous, intraperitoneal, intramuscular). The compound can be administered by intravenous infusion or injection. The compound can be administered by intramuscular or subcutaneous injection.

Oral administration of a solid dosage form may be, for example, presented in discrete units, such as hard or soft capsules, pills, cachets, lozenges, or tablets, each containing a predetermined amount of at least one compound of the disclosure. The oral administration may be in a powder or granule form. The oral dosage form can be sub-lingual, for example, a lozenge. In such solid dosage forms, the compounds of the disclosure are ordinarily combined with one or more adjuvants. Such capsules or tablets may comprise a controlled release formulation. In the case of capsules, tablets, and pills, the dosage forms also may comprise buffering agents or may be prepared with enteric coatings.

Oral administration may be in a liquid dosage form. Liquid dosage forms for oral administration include, for example, pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs containing inert diluents commonly used in the art (e.g., water). Such compositions also may comprise adjuvants, such as one or more of wetting, emulsifying, suspending, flavoring (e.g., sweetening), or perfuming agents.

The disclosure comprises a parenteral dosage form. "Parenteral administration" includes, for example, subcutaneous injections, intravenous injections, intraperitoneally, intramuscular injections, intrasternal injections, and infusion. Injectable preparations (i.e., sterile

injectable aqueous or oleaginous suspensions) may be formulated according to the known art using one or more of suitable dispersing, wetting agents, or suspending agents.

The disclosure comprises a topical dosage form. "Topical administration" includes, for example, dermal and transdermal administration, such as via transdermal patches or iontophoresis devices, intraocular administration, or intranasal or inhalation administration. Compositions for topical administration also include, for example, topical gels, sprays, ointments, and creams. A topical formulation may include a compound which enhances absorption or penetration of the active ingredient through the skin or other affected areas. When the compounds of the disclosure are administered by a transdermal device, administration will be accomplished using a patch either of the reservoir and porous membrane type or of a solid matrix variety. Typical formulations for this purpose include gels, hydrogels, lotions, solutions, creams, ointments, dusting powders, dressings, foams, films, skin patches, wafers, implants, sponges, fibers, bandages and microemulsions. Liposomes may also be used. Typical excipients include alcohol, water, mineral oil, liquid petrolatum, white petrolatum, glycerin, polyethylene glycol and propylene glycol. Penetration enhancers may be incorporated - see, for example, B. C. Finnin and T. M. Morgan, J. Pharm. Sci., vol. 88, pp. 955-958, 1999.

Formulations suitable for topical administration to the eye include, for example, eye drops wherein the compound of the disclosure is dissolved or suspended in a suitable excipient. A typical formulation suitable for ocular or aural administration may be in the form of drops of a micronized suspension or solution in isotonic, pH-adjusted, sterile saline. Other formulations suitable for ocular and aural administration include ointments, biodegradable (i.e., absorbable gel sponges, collagen) and non-biodegradable (i.e., silicone) implants, wafers, lenses and particulate or vesicular systems, such as niosomes or liposomes. A polymer such as crossed linked polyacrylic acid, polyvinyl alcohol, hyaluronic acid, a cellulosic polymer, for example, hydroxypropylmethylcellulose, hydroxyethylcellulose, or methylcellulose, or a heteropolysaccharide polymer, for example, gelan gum, may be incorporated together with a preservative, such as benzalkonium chloride. Such formulations may also be delivered by iontophoresis.

For intranasal administration, the compounds of the disclosure are conveniently delivered in the form of a solution or suspension from a pump spray container that is squeezed or pumped by the patient or as an aerosol spray presentation from a pressurized container or a nebulizer, with the use of a suitable propellant. Formulations suitable for intranasal administration are typically administered in the form of a dry powder (either alone, as a mixture, for example, in a dry blend with lactose, or as a mixed component particle, for example, mixed with phospholipids, such as phosphatidylcholine) from a dry powder inhaler or as an aerosol spray from a pressurized container, pump, spray, atomizer (preferably an atomizer using electrohydrodynamics to produce a fine mist), or nebulizer, with or without the use of a suitable

propellant, such as 1,1,1,2-tetrafluoroethane or 1,1,1,2,3,3,3-heptafluoropropane. For intranasal use, the powder may comprise a bioadhesive agent, for example, chitosan or cyclodextrin.

The disclosure comprises a rectal dosage form. Such rectal dosage form may be in the form of, for example, a suppository. Cocoa butter is a traditional suppository base, but various alternatives may be used as appropriate.

Other excipients and modes of administration known in the pharmaceutical art may also be used. Pharmaceutical compositions of the disclosure may be prepared by any of the well-known techniques of pharmacy, such as effective formulation and administration procedures. The above considerations in regard to effective formulations and administration procedures are well known in the art and are described in standard textbooks. Formulation of drugs is discussed in, for example, Ansel, Howard C., *et al.*, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Philadelphia: Lippincott, Williams & Wilkins, 2004; Gennaro, Alfonso R., *et al.* Remington: The Science and Practice of Pharmacy. Philadelphia: Lippincott, Williams & Wilkins, 2000; Rowe, Raymond C. Handbook of Pharmaceutical Excipients. Chicago, Pharmaceutical Press, 2005; Stahl, P. Heinrich and Camilli G. Wermuth, Eds. Handbook of Pharmaceutical Salts: Properties, Selection, and Use. New York: Wiley-VCH, 2011; and Brittain, Harry G., Ed. Polymorphism in Pharmaceutical Solids. New York: Informa Healthcare USA, Inc., 2016.

Acceptable excipients are nontoxic to subjects at the dosages and concentrations employed, and may comprise one or more of the following: 1) buffers such as phosphate, citrate, or other organic acids; 2) salts such as sodium chloride; 3) antioxidants such as ascorbic acid or methionine; 4) preservatives such as octadecyldimethylbenzyl ammonium chloride, hexamethonium chloride, benzalkonium chloride, benzethonium chloride, phenol, butyl or benzyl alcohol; 5) alkyl parabens such as methyl or propyl paraben, catechol, resorcinol, cyclohexanol, 3-pentanol, or m-cresol; 6) low molecular weight (less than about 10 residues) polypeptides; 7) proteins such as serum albumin, gelatin, or immunoglobulins; 8) hydrophilic polymers such as polyvinylpyrrolidone; 9) amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; 10) monosaccharides, disaccharides, or other carbohydrates including glucose, mannose, or dextrins; 11) chelating agents such as EDTA; 12) sugars such as sucrose, mannitol, trehalose or sorbitol; 13) salt-forming counter-ions such as sodium, metal complexes (e.g., Zn-protein complexes), or 14) non-ionic surfactants such as polysorbates (e.g., polysorbate 20 or polysorbate 80), poloxamers or polyethylene glycol (PEG).

For oral administration, the compositions may be provided in the form of tablets or capsules containing 0.01, 0.05, 0.1, 0.5, 1.0, 2.5, 5.0, 10.0, 15.0, 25.0, 50.0, 75.0, 100, 125, 150, 175, 200, 250, or 500 milligrams (mg) of the active ingredient for the symptomatic adjustment of the dosage to the patient. A medicament typically contains 0.01 mg to 500 mg of the active ingredient, or 1 mg to 100 mg of active ingredient. Intravenous doses may be in the range of 0.01 to 10 mg/kg/minute during a constant rate infusion.

Liposome containing compounds of the disclosure may be prepared by methods known in the art (See, for example, Chang, H.I.; Yeh, M.K.; Clinical development of liposome-based drugs: formulation, characterization, and therapeutic efficacy; Int J Nanomedicine 2012; 7; 49-60). Particularly useful liposomes may be generated by the reverse phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter.

Compounds of the disclosure may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington, The Science and Practice of Pharmacy, 20th Ed., Mack Publishing (2000).

Sustained-release preparations may be used. Suitable examples of sustained-release preparations include semi-permeable matrices of solid hydrophobic polymers containing a compound of the disclosure, which matrices are in the form of shaped articles, e.g., films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate) or poly(vinylalcohol)), polylactides, copolymers of L-glutamic acid and 7 ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as those used in leuprolide acetate for depot suspension (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), sucrose acetate isobutyrate, and poly-D-(-)-3-hydroxybutyric acid.

The formulations to be used for intravenous administration must be sterile. This is readily accomplished by, for example, filtration through sterile filtration membranes. Compounds of the disclosure are generally placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Suitable emulsions may be prepared using commercially available fat emulsions, such as a lipid emulsion comprising soybean oil, a fat emulsion for intravenous administration (e.g., comprising safflower oil, soybean oil, egg phosphatides and glycerin in water), emulsions containing soya bean oil and medium-chain triglycerides, and lipid emulsions of cottonseed oil. The active ingredient may be either dissolved in a pre-mixed emulsion composition or alternatively it may be dissolved in an oil (e.g., soybean oil, safflower oil, cottonseed oil, sesame oil, corn oil or almond oil) and an emulsion formed upon mixing with a phospholipid (e.g., egg phospholipids, soybean phospholipids or soybean lecithin) and water. It will be appreciated that other ingredients may be added, for example glycerol or glucose, to adjust the tonicity of the emulsion. Suitable emulsions will typically contain up to 20% oil, for example, between 5 and

20%. The fat emulsion may comprise fat droplets having a diameter of 0.1 to 1.0 micrometers (μm), particularly 0.1 to 0.5 μm, and have a pH of 5.5 to 8.0.

For example, the emulsion compositions may be those prepared by mixing a compound of the disclosure with a lipid emulsion comprising soybean oil or the components thereof (soybean oil, egg phospholipids, glycerol and water).

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

A drug product intermediate (DPI) is a partly processed material that must undergo further processing steps before it becomes bulk drug product. Compounds of the disclosure may be formulated into drug product intermediate DPI containing the active ingredient in a higher free energy form than the crystalline form. One reason to use a DPI is to improve oral absorption characteristics due to low solubility, slow dissolution, improved mass transport through the mucus layer adjacent to the epithelial cells, and in some cases, limitations due to biological barriers such as metabolism and transporters. Other reasons may include improved solid state stability and downstream manufacturability. The drug product intermediate can contain a compound of the disclosure isolated and stabilized in the amorphous state (for example, amorphous solid dispersions (ASDs)). There are many techniques known in the art to manufacture ASD's that produce material suitable for integration into a bulk drug product, for example, spray dried dispersions (SDD's), melt extrudates (often referred to as HME's), co-precipitates, amorphous drug nanoparticles, and nano-adsorbates. Amorphous solid dispersions can comprise a compound of the disclosure and a polymer excipient. Other excipients as well as concentrations of said excipients and the compound of the disclosure are well known in the art and are described in standard textbooks. See, for example, "*Amorphous Solid Dispersions Theory and Practice*" by Navnit Shah et al.

This disclosure further comprises use of a compound of the disclosure for use as a medicament (such as a unit dosage tablet or unit dosage capsule). This disclosure comprises the use of a compound of the disclosure for the manufacture of a medicament (such as a unit dosage tablet or unit dosage capsule) to treat one or more of the conditions previously identified in the above sections discussing methods of treatment. This disclosure further comprises a compound of the disclosure, or a pharmaceutically acceptable salt thereof, for use as a

medicament and a compound the disclosure, or a pharmaceutically acceptable salt therefore, for use in any method of treatment herein disclosed.

Typically, a compound of the disclosure is administered in an amount effective to treat a condition as described herein. The compounds of the disclosure may be administered as compound per se, or alternatively, as a pharmaceutically acceptable salt. For administration and dosing purposes, the compound per se or pharmaceutically acceptable salt thereof will simply be referred to as the compounds of the disclosure.

The compounds of the disclosure are administered by any suitable route in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended. The compounds of the disclosure may be administered orally, rectally, vaginally, parenterally, topically, intranasally, or by inhalation.

The compounds of the disclosure may be administered orally. Oral administration may involve swallowing, so that the compound enters the gastrointestinal tract, or buccal or sublingual administration may be employed by which the compound enters the bloodstream directly from the mouth.

The compounds of the disclosure may also be administered parenterally, for example, directly into the bloodstream, into muscle, or into an internal organ. Suitable means for parenteral administration include intravenous, intraarterial, intraperitoneal, intrathecal, intraventricular, intraurethral, intrasternal, intracranial, intramuscular, and subcutaneous. Suitable devices for parenteral administration include needle (including microneedle) injectors, needle-free injectors, and infusion techniques.

The compounds of the disclosure may be administered topically to the skin or mucosa, that is, dermally or transdermally. The compounds of the disclosure may also be administered intranasally or by inhalation. The compounds of the disclosure may be administered rectally or vaginally. The compounds of the disclosure may also be administered directly to the eye or ear.

The dosage regimen for the compounds of the disclosure or compositions containing said compounds is based on a variety of factors, including the type, age, weight, sex and medical condition of the patient; the severity of the condition; the route of administration; and the activity of the particular compound employed. Thus, the dosage regimen may vary widely. The total daily dose of a compound of the disclosure can be 0.01 to 100 mg/kg (i.e., mg compound of the disclosure per kg body weight) for the treatment of the indicated conditions discussed herein. The total daily dose of the compound of the disclosure can be 0.1 to 50 mg/kg, or 0.5 to 30 mg/kg. It is not uncommon that the administration of the compounds of the disclosure will be repeated a plurality of times in a day (typically no greater than 4 times). Multiple doses per day typically may be used to increase the total daily dose, if desired.

The compounds of the disclosure may inhibit the activity of STAT6 and may be useful in the treatment, prevention, suppression, and amelioration of disease(s) or diseases, disorders, and conditions mediated by STAT6.

The compounds of the disclosure may be used to treat or prevent at least one disease or condition relating to an inflammatory disorder. The compounds of the disclosure may be used to treat or prevent at least one disease or condition including atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy (including food allergy, latex allergy, pet allergy, mold allergy, insect allergy, pollen allergy, dust allergy, seasonal allergy, ragweed allergy, drug allergy, allergic rhinitis, allergic rhinitis, allergic fungal rhinosinusitis, allergic contact dermatitis, and allergic bronchopulmonary aspergillosis), alopecia (including alopecia areata), Alzheimer's disease, arteritis, asthma, atherosclerosis, autoimmune disorders (including lupus nephritis, autoimmune hepatitis, myasthenia gravis, Guillain-Barre syndrome, and Graves' disease) Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease, chronic pruritis, chronic urticaria, celiac disease, Crohn's disease (CD), dermatitis (including atopic dermatitis (AD), hand dermatitis, and hand or foot atopic dermatitis), diabetic kidney disease, diversion colitis, eosinophilic esophagitis (including pediatric eosinophilic esophagitis), eye disorders or conditions (including autoimmune diseases of the eye, keratoconjunctivitis, vernal conjunctivitis, non-infectious uveitis (e.g. uveitis associated with Bechet's disease and lens-induced uveitis), keratitis (e.g. herpetic keratitis and conical keratitis), keratoleukoma, ocular premphigus, Mooren's ulcer, scleritis, retinitis, retinopathy, Grave's ophthalmopathy, Vogt-Koyanagi-Harada syndrome, keratoconjunctivitis sicca (dry eye), phlyctenule, iridocyclitis, endocrine ophthalmopathy, sympathetic ophthalmitis, allergic conjunctivitis, and ocular neovascularization), fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), indeterminate colitis, keloids, mastocytosis, microscopic colitis (such as collagenous colitis or lymphocytic colitis), myositis, nephritis, non-alcoholic steatohepatitis (NASH), pancreatitis, primary biliary cirrhosis, proctitis, prurigo nodularis, psoriasis, psoriatic arthritis, primary biliary cirrhosis, rhinosinusitis (including chronic rhinosinusitis with or without nasal polyps), sarcoidosis, scleroderma, sclerosing cholangitis, Sjogren's syndrome, systemic lupus erythematosus (SLE), systemic sclerosis, thyroiditis, ulcerative colitis (UC), vitiligo, vasculitis, Vogt-Koyanagi-Harada syndrome, Wegener's granulomatosis, or hidradenitis suppurativa. A method of treating or preventing one or one or more symptoms associated with the respective disease or condition comprises administering a pharmaceutical composition comprising a therapeutically effective amount of a compound of the disclosure to a patient.

The compounds of the disclosure may be used to treat or prevent at least one disease or condition including atopic dermatitis, asthma, chronic obstructive pulmonary disease (COPD), rhinosinusitis (for example, chronic rhinosinusitis with nasal polyps or chronic rhinosinusitis without nasal polyps), chronic urticaria (for example, chronic inducible urticaria or chronic spontaneous urticaria), prurigo nodularis, eosinophilic esophagitis, eosinophilic gastritis, bullous pemphigoid, pruritis (for example, chronic pruritis of unknown origin), atopic keratoconjunctivitis, chronic inducible urticaria, or allergy (for example, food allergy).

The compounds of the disclosure may be used to treat or prevent dermatological conditions, such as eczema (e.g. chronic and dyshidrotic eczema), chronic itch, dermatitis (e.g. atopic, irritant contact, allergic contact, occupational, perioral, stasis, nummular, seborrheic, xerotic, eyelid, diaper, and hand dermatitis), vitiligo, alopecia, alopecia areata, pruritis (e.g. chronic idiopathic pruritus), prurigo nodularis, psoriasis (e.g. plaque, guttate, inverse, pustular, nail, flexural palmoplantar, facial or erythrodermic psoriasis), scleroderma, pemphigus, dermatomyositis, neurodermatitis, skin flushing, cutaneous lupus erythematosus (e.g. acute cutaneous lupus (acute skin lupus), subacute cutaneous lupus (subacute lupus), and chronic cutaneous lupus (discoid lupus)), keloid, sunburn, hypertrophic scar, idiopathic thrombocytopenic purpura (ITP), ichthyosis (e.g. ichthyosis vulgaris), epidermal hyperplasia, acne, lichen planus, lichen sclerosis, rosacea, epidermolysis bullosa, intertrigo, keratosis pilaris, urticaria (e.g. chronic spontaneous urticaria, chronic idiopathic urticaria, chronic physical urticaria), molluscum contagiosum, Netherton syndrome, Sweet's syndrome, pityriasis alba, vulvovaginitis, Sutton's nevus/nevi, post inflammatory hypopigmentation, senile leukoderma, chemical/drug-induced leukoderma, palmoplantar pustulosis, pemphigoid, pemphigoid nodularis, bullous pemphigoid, and hidradenitis suppurativa.

The compounds of the disclosure may be used to treat or prevent respiratory conditions, such as rhinitis (e.g. allergic and perennial rhinitis), rhinorrhea, nasal congestion, nasal inflammation, asthma (e.g. chronic asthma, inveterate asthma, late asthma, bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, and dust asthma), chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), chronic and acute bronchoconstriction, chronic bronchitis, emphysema, allergic bronchopulmonary aspergillosis, chronic eosinophilic pneumonia, acute lung injury (ACI), adult respiratory distress syndrome (ARDS), pulmonary vascular disease (PVD), pulmonary arterial hypertension (PAH), bronchiectasis, sinusitis, rhinosinusitis, allergic fungal rhinosinusitis, chronic rhinosinusitis with nasal polyps, pulmonary sarcoidosis, and silicosis.

The compounds of the disclosure may be used to treat or prevent joint disorders, such as arthritis (e.g. osteoarthritis, as well as psoriatic, rheumatoid, juvenile, and gouty arthritis), spondyloarthropathy (e.g. reactive arthritis (also known as Reiter's Syndrome) and axial spondyloarthritis (including ankylosing spondylitis)), cartilage inflammation, bone degradation, and Still's disease; cardiovascular and metabolic disorders, such as diabetes (type 1 and type 2), myocarditis, diabetic neuropathy, atherosclerosis, cachexia, and celiac sprue; neuroinflammatory disorders, such as lupus (e.g. CNS, systemic and discoid lupus), systemic lupus erythematosus (SLE), diabetic neuropathy, autoimmune encephalitis, Alzheimer's disease, Parkinson's disease, and multiple sclerosis; and cancer.

The compound of the disclosure may be used alone, or in combination with one or more other therapeutic agents. The disclosure provides any of the uses, methods or compositions as

defined herein wherein the compound of the disclosure, or pharmaceutically acceptable salt thereof, is used in combination with one or more other therapeutic agent discussed herein.

The administration of two or more compounds "in combination" means that all of the compounds are administered closely enough in time to affect treatment of the subject. The two or more compounds may be administered simultaneously or sequentially, via the same or different routes of administration, on same or different administration schedules and with or without specific time limits depending on the treatment regimen. Additionally, simultaneous administration may be carried out by mixing the compounds prior to administration or by administering the compound at the same point in time but as separate dosage forms at the same or different site of administration. Examples of "in combination" include, but are not limited to, "concurrent administration," "co-administration," "simultaneous administration," "sequential administration" and "administered simultaneously".

A compound of the disclosure and the one or more other therapeutic agents may be administered as a fixed or non-fixed combination of the active ingredients. The term "fixed combination" means a compound of the disclosure, or a pharmaceutically acceptable salt thereof, and the one or more therapeutic agents, are both administered to a subject simultaneously in a single composition or dosage. The term "non-fixed combination" means that a compound of the disclosure, or a pharmaceutically acceptable salt thereof, and the one or more therapeutic agents are formulated as separate compositions or dosages such that they may be administered to a subject in need thereof simultaneously or at different times with variable intervening time limits, wherein such administration provides effective levels of the two or more compounds in the body of the subject.

The compounds of the disclosure can be administered in combination with one or more pharmaceutically active agents other than the compounds of the disclosure including the pharmaceutically acceptable salts of the specifically named agents and the pharmaceutically acceptable solvates of said agents and salts.

The present disclosure can provide a pharmaceutical composition comprising the compound of the disclosure or a pharmaceutically acceptable salt thereof, wherein the pharmaceutical composition is administered in combination with a pharmaceutical composition comprising a different pharmaceutically active compound or a pharmaceutically acceptable salt thereof simultaneously or at different times.

These agents and compounds may be combined with pharmaceutically acceptable vehicles such as saline, Ringer's solution, dextrose solution, and the like. The particular dosage regimen, i.e., dose, timing and repetition, will depend on the particular individual and that individual's medical history.

Another aspect of the disclosure provides kits comprising the compound of the disclosure or pharmaceutical compositions comprising the compound . A kit may include, in addition to the compound of the disclosure or pharmaceutical composition thereof, diagnostic or

therapeutic agents. A kit may also include instructions for use in a diagnostic or therapeutic method. The kit can include the compound or a pharmaceutical composition thereof and a diagnostic agent. The kit can include the compound or a pharmaceutical composition thereof and one or more therapeutic agents.

The kits can be suitable for use in performing the methods of treatment described herein. The kit can contain a first dosage form comprising one or more of the compounds of the disclosure in quantities sufficient to carry out the methods of the disclosure. The kit can comprise one or more compounds of the disclosure in quantities sufficient to carry out the methods of the disclosure and a container for the dosage and a container for the dosage.

Compounds of the present disclosure may be synthesized by synthetic routes that include processes analogous to those well-known in the chemical arts, particularly in light of the description contained herein. The starting materials are generally available from commercial sources or may be prepared using methods well known to those skilled in the art. Many of the compounds used herein, are related to, or may be derived from compounds in which one or more of the scientific interest or commercial need has occurred. Accordingly, such compounds may be one or more of 1) commercially available; 2) reported in the literature or 3) prepared from other commonly available substances by one skilled in the art using materials which have been reported in the literature.

For illustrative purposes, the reaction schemes depicted below provide potential routes for synthesizing the compounds of the present disclosure as well as key intermediates. For a more detailed description of the individual reaction steps, see the Examples section below. Those skilled in the art will appreciate that other synthetic routes may be used to synthesize the inventive compounds. Although specific starting materials and reagents are discussed below, other starting materials and reagents may be substituted to provide one or more of a variety of derivatives or reaction conditions. In addition, many of the compounds prepared by the methods described below may be further modified in light of this disclosure using conventional chemistry well known to those skilled in the art.

The skilled person will appreciate that the experimental conditions set forth in the schemes that follow are illustrative of suitable conditions for effecting the transformations shown, and that it may be necessary or desirable to vary the precise conditions employed for the preparation of compounds of Formula I. It will be further appreciated that it may be necessary or desirable to carry out the transformations in a different order from that described in the schemes, or to modify one or more of the transformations, to provide the desired compound of Formula I.

In the preparation of compounds of Formula I it is noted that some of the preparation methods useful for the preparation of the compounds described herein may require protection of remote functionality (e.g., a primary amine, secondary amine, carboxyl, etc. in a precursor of a compound of Formula I). The need for such protection will vary depending on the nature of

the remote functionality and the conditions of the preparation methods. The need for such protection is readily determined by one skilled in the art. The use of such protection/deprotection methods is also within the skill in the art. For a general description of protecting groups and their use, see March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure 8th Edition.

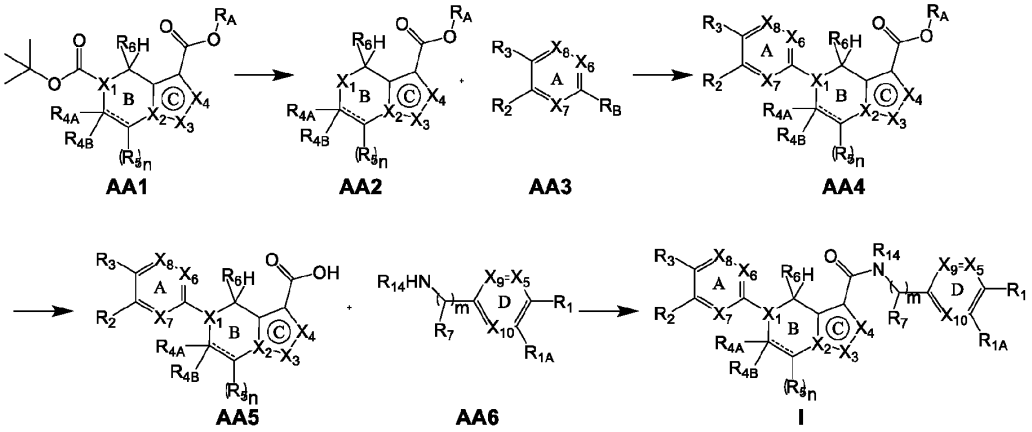
For example, if a compound contains amine or carboxylic acid functionality, such functionality may interfere with reactions at other sites of the molecule if left unprotected. Accordingly, such functionalities may be protected by an appropriate protecting group (PG) that may be removed in a subsequent step. Suitable protecting groups for amine and carboxylic acid protection include those protecting groups commonly used in peptide synthesis (such as *N*-t-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), and 9-fluorenylmethylenoxycarbonyl (Fmoc) for amines and lower alkyl or benzyl esters for carboxylic acids) that are generally not chemically reactive under the reaction conditions described and may typically be removed without chemically altering other functionality in a compound of Formula I.

One skilled in the art will recognize that, in some cases, the compounds will be generated as a mixture of diastereomers and/or enantiomers; these may be separated at various stages of the synthetic scheme using conventional techniques or a combination of such techniques, such as, but not limited to, crystallization, normal-phase chromatography, reversed-phase chromatography and chiral chromatography, to afford the single enantiomers of the disclosure; for example, see "Stereochemistry of Organic Compounds" by E. L. Eliel and S. H. Wilen (Wiley, New York, 1994).

Unless otherwise indicated, the substituents in the schemes are defined as above. Isolation and purification of the products are accomplished by standard procedures, which are known to a chemist of ordinary skill.

It will be understood by one skilled in the art that the various symbols, superscripts, and subscripts used in the schemes, methods, and examples are used for the convenience of representation and/or to reflect the order in which they are introduced in the schemes and are not intended to necessarily correspond to the symbols, superscripts or subscripts in the appended claims. The schemes are representative of methods useful in synthesizing the compounds of the present disclosure. They are not to constrain the scope of the disclosure in any way.

General Scheme A



The general structure of Formula **I** can be prepared as shown in General Scheme A. The *tert*-butyloxycarbonyl (BOC) protected amine of Formula **AA1**, synthesized by literature methods or purchased commercially, can be treated with standard acidic deprotection reagents such as hydrochloric acid (HCl) in solvents like 1,4-dioxane (dioxane), ethyl acetate (EtOAc) and dichloromethane (DCM) from 10 degrees Celsius (°C) to room temperature to afford the deprotected amine compound of Formula **AA2**. The amine of Formula **AA2** can be treated with a halogen (e.g., R_B= F or Br)-substituted aromatic of Formula **AA3** using standard S_NAr conditions such as *N,N*-diisopropylethylamine (DIEA), tripotassium phosphate (K_3PO_4), potassium carbonate (K_2CO_3), or cesium fluoride (CsF) in 1-pentanol, butyronitrile, dimethylformamide (DMF), dimethyl sulfoxide (DMSO), or acetonitrile (ACN) when heated between 80 to 140 °C to afford Formula **AA4**. The Formula **AA4** can also be prepared by reacting Formula **AA2** and **AA3** with copper(I) iodide (CuI), 1,2-dimethylethylenediamine (DMEDA), or trans-N,N′-dimethylcyclohexane-1,2-diamine or Pd catalyst such as (2-dicyclohexylphosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate (RuPhos Pd G3) with 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl (RuPhos), mesylate[(di(1-adamantyl)-n-butylphosphine)-2-(2′-amino-1,1′-biphenyl)]palladium(II) (cataCXium® A Pd G3), [dicyclohexyl(2′,6′-diisopropoxy-2-biphenylyl)phosphine-κ*P*](methanesulfonatato-κ*O*)[2′-(methylamino-κ*N*)-2-biphenylyl-κC^2]palladium (RuPhos Pd G4) with a base such as sodium *tert*-butoxide (NaO*t*Bu), K_2CO_3, tripotassium phosphate (K_3PO_4) or cesium carbonate (Cs_2CO_3) in a solvent like dioxane, dimethylacetamide (DMA), DMF, DMSO, 2-methyl-2-butanol (*tert*-amyl alcohol) or toluene and heated between 80 to 130 °C.

Formula **AA4**, where R_3 is a halogen (e.g., F, Br, or I), can be converted to an amine, urea, or lactam using standard SNAr or cross coupling conditions described above to afford Formula **AA4**. When R_3 is a halogen (e.g. I) on Formula **AA4**, the halogen can react with a BOC-protected hydrazine with the cross coupling conditions described above then can be deprotected under standard acidic conditions such as HCl in a solvent like dioxane or DCM and cyclized by reacting with (*E*)-4-(dimethylamino)but-3-en-2-one in EtOH to converted R_3 to a 5-

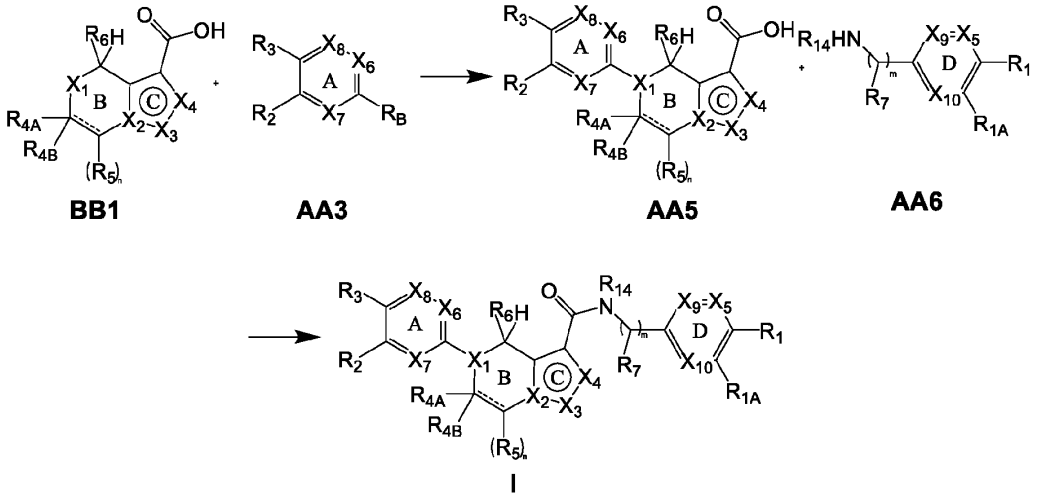
methyl-1*H*-pyrazole on Formula **AA4**. For Formula **AA4**, where R_3 is a halogen (e.g., Br, I), can be converted to a carbon-carbon bond by reacting the halogen with nickel(II) chloride ethylene glycol dimethyl ether complex ($NiCl_2$.glyme), 5-methoxypicolinimidamide, and using activated ester of *N*-hydroxyphthalimide, tetrabutylammonium iodide, preactivated zinc (Zn) and trifluoroacetic acid (TFA) in a solvent like DMA from room temperature to 70 °C or under photoredox conditions such as [4,4′-b*is*(1,1-dimethylethyl)-2,2′-bipyridine-*N*1,*N*1′]*bis*[2-(2-pyridinyl-*N*)phenyl-C]iridium(III) hexafluorophosphate ($Ir(ppy)_2(dtbbpy)PF_6$), nickel(II) bromide ethylene glycol dimethyl ether complex ($NiBr_2$.DME), 5-methoxypicolinimidamide, phthalimide and quinuclidine in a solvent such as DMA and methyl tertiary-butyl ether (MTBE) to afford Formula **AA4**. When R_3 is a halogen (e.g. Br) on Formula **AA4**, the halogen can react with B_2Pin_2 and $Pd(dppf)Cl_2$ with a base like KOAc in a solvent like dioxane at 85 °C to form boronic acid at R_3. The boronic acid at R_3 can react further by reacting with bromo-substituted 5-membered ring heterocycle, $Pd(dppf)Cl_2$ and with a base like K_3PO_4 in solvents like dioxane at 85 °C to give a 5-membered ring heterocycle at R_3 on Formula **AA4**. When R_3 is a carboxylic acid on Formula **AA4**, the acid can be transformed further via amide coupling with HATU and a base like DIEA in a solvent like DMF at 40 °C to form the amide on R_3. When R_3 is a *tert*-butyl acetate on Formula **AA4**, it can be deprotected under standard acidic conditions such as TFA or HCl in a solvent like dioxane, H2O, and DCM from room temperature to 40 °C, then transformed further under standard amide coupling conditions to form an amide at R_3. When R_3 is a methyl propionate on Formula **AA4** then Formula **AA4** can react with 2-bromoacetonitrile with a base like lithium bis(trimethylsilyl)amide (LiHMDS) in a solvent like THF at -78 °C which can be transformed further by reacting with sodium borohydride ($NaBH_4$) in solvents like THF and H_2O at 0 °C to room temperature to form a 5-membered lactam at R_3 on Formula **AA4**.

The ester (e.g., R_A= methyl or ethyl) of Formula **AA4** can undergo standard hydrolysis conditions such as utilizing a base (e.g., lithium hydroxide monohydrate (LiOH), sodium hydroxide (NaOH), 1,5,7-triazabicyclo[4.4.0]dec-5-ene, or potassium trimethylsilanolate (KOTMS) in solvents like tetrahydrofuran (THF), methanol (MeOH), ethanol (EtOH), water (H_2O), dioxane, or ACN. The reaction can typically occur at 0 to 50 °C, preferably at about 23 °C (room temperature), to afford the carboxylic acid of Formula **AA5**. The compound of Formula **I** can be obtained by reacting the carboxylic acid of **AA5** with the amine of Formula **AA6** under standard amide coupling reagents like 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) with 2-hydroxypyridine-N-oxide (HOPO), 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate (HATU), or other common reagents in solvents such as ACN and H_2O, DMF, or DMSO along with an organic base such as triethylamine (TEA) or DIEA stirred at a temperature of 0 to 70 °C, preferably at about 23 °C (room temperature).

In Formula **I**, when R_1 is an amine, it can react with 2,2,2-trichloroethyl carbonochloridate in pyridine from 0 °C to room temperature, then transform further with a

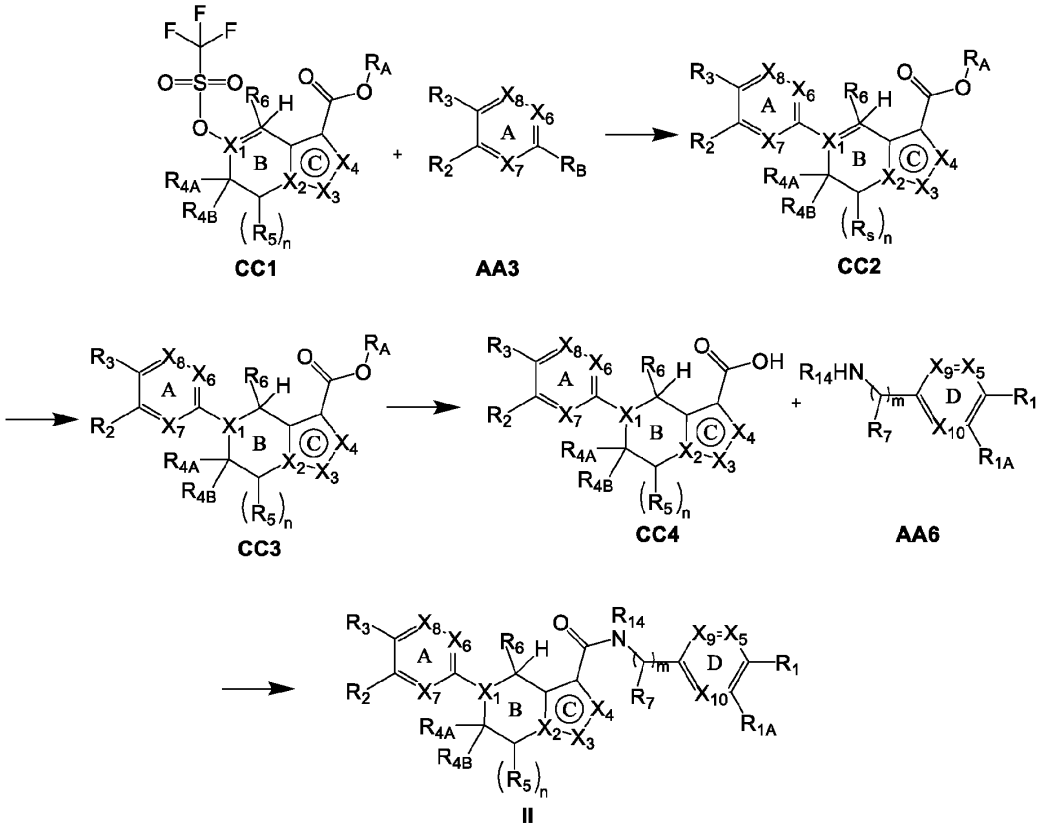
secondary amine and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in THF from 40-60 °C to form a urea at R_3. In Formula **I**, when R_1 is phenyl carbamate, it can react with an amine and a base like TEA in a solvent like DMF from 40 °C, then deprotected under acidic conditions with HCl in a solvent like dioxane and DCM from 0 °C to room temperature to form a urea at R_3. In Formula **I**, when R_3 is a *tert*-butyl acetate, it can be deprotected under standard acidic conditions, such as HCl in a solvent like H_2O and DCM. In Formula **I**, when R_1 is an amine, it can react with ethyl carbonochloridate with a base like TEA in a solvent like DCM from 0 °C to room temperature to form an amide at R_3.

General Scheme B



The general structure of Formula **I** can be prepared as shown in General Scheme B. The amine of Formula **BB1** can be treated with a halogen (e.g., R_B= F or Cl)-substituted aromatic of Formula **AA3** using standard SNAr conditions such as cesium fluoride (CsF) or K_3PO_4 in a solvent like water or DMSO and stirred at 80 to 140 °C to afford Formula **AA5**. The compound of Formula **I** can be obtained by reacting the carboxylic acid of **AA5** with the amine of Formula **AA6** under standard amide coupling reagents like EDCI with HOPO, HATU, or other common amide coupling reagents in solvents such as ACN and H_2O, DMF, or DMSO along with an organic base such as TEA or DIEA stirred at a temperature of 0 to 70 °C, preferably at room temperature. In Formula **I,** when R_6 is a hydrogen, can be oxidized with 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) in acetone and then further transformed to methylate when reacted with boron trifluoride diethyl etherate (BF_3OEt_2) and dimethylzinc in solvents like toluene and THF. In Formula **I,** when R_3 is a *tert*-butyl acetate, can be deprotected under standard acidic conditions, such as HCl in a solvent like dioxane, H_2O, and DCM, then transformed further under standard amide coupling conditions to form an amide at R_3.

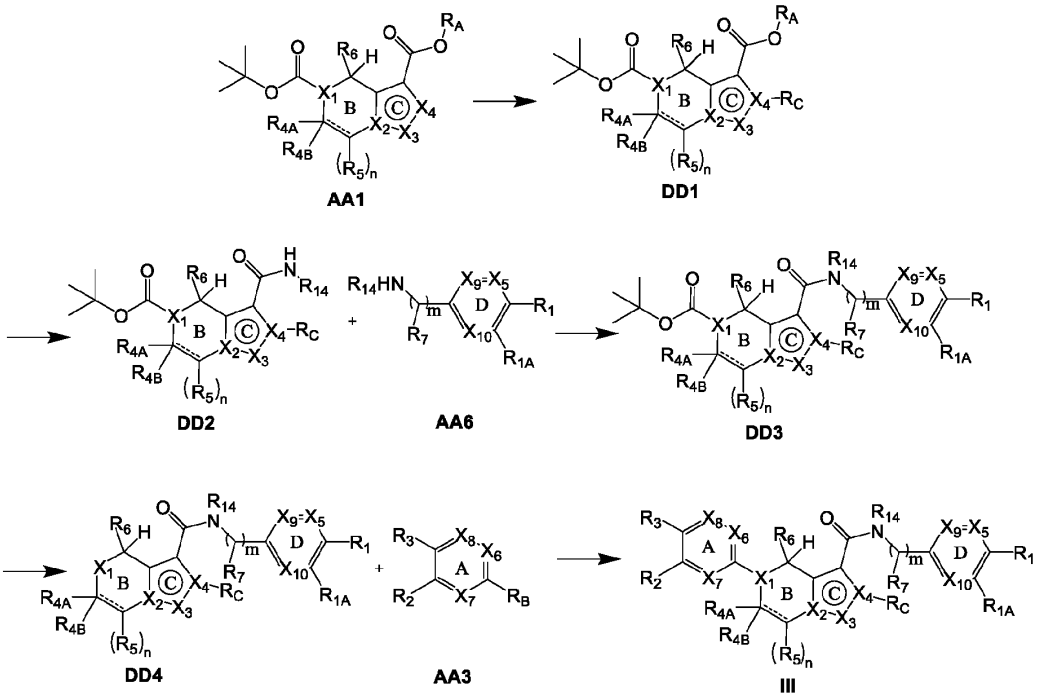
General Scheme C



The general structure of Formula **II** can be prepared as shown in General Scheme C. The trifluoromethanesulfonic acid of Formula **CC1**, synthesized by literature methods or purchased commercially, can be treated with a boronic acid (e.g. R_B= B-$(OH)_2$)-substituted aromatic of Formula **AA3** using with a Pd catalyst such as Pd(dppf)Cl_2 and a base like K_3PO_4 in solvents such as H_2O and THF at 85 °C to form Formula **CC2**. The alkene of Formula **CC2** can undergo hydrogenation with palladium on carbon (Pd/C) in EtOH to reduce the alkene to form Formula **CC3**. The ester (e.g., R_A= ethyl) of Formula **CC3** can undergo standard hydrolysis conditions by utilizing a base like LiOH in solvents like THF, MeOH and H_2O from 0 to 50 °C, preferably at room temperature, to afford the carboxylic acid of Formula **CC4**. The compound of Formula **II** can be obtained by reacting the carboxylic acid of **CC4** with the amine of Formula **AA6** under standard amide coupling reagents like EDCI with HOPO in solvents such as DMSO along with an organic base such as DIEA stirred at 0 to 70 °C.**II** can be prepared as shown in General Scheme C. The trifluoromethanesulfonic acid of Formula **CC1**, synthesized by literature methods or purchased commercially, can be treated with a boronic acid (e.g. R_B= B-$(OH)_2$)-substituted aromatic of Formula **AA3** using with a Pd catalyst such as Pd(dppf)Cl_2 and a base like K_3PO_4 in solvents such as H_2O and THF at 85 °C to form Formula **CC2**. The alkene of Formula **CC2** can undergo hydrogenation with palladium on carbon (Pd/C) in EtOH to reduce

the alkene to form Formula **CC3**. The ester (e.g., R_A= ethyl) of Formula **CC3** can undergo standard hydrolysis conditions by utilizing a base like LiOH in solvents like THF, MeOH and H_2O from 0 to 50 °C, preferably at room temperature, to afford the carboxylic acid of Formula **CC4**. The compound of Formula **II** can be obtained by reacting the carboxylic acid of **CC4** with the amine of Formula **AA6** under standard amide coupling reagents like EDCI with HOPO in solvents such as DMSO along with an organic base such as DIEA stirred at 0 to 70 °C.

General Scheme D



The general structure of Formula **III** can be prepared as shown in General Scheme D. The BOC protected amine of Formula **AA1**, synthesized by literature methods or purchased commercially, which can be treated with bromo substituted alkyl amine protected as benzyloxy carbonyl (Cbz) with a base like Cs_2CO_3 in ACN to give mixture of N1 and N2-alkylated (e.g. R_C= Cbz protected alkyl amine) compounds of Formula **DD1.** The regioisomers can be separated by silica gel column purification to provide compounds of Formula **DD2.** Formula **DD2** can then undergo deprotection of the CBz protecting group with reducing conditions such as Pd/C in a solvent like EtOH at 50-120 pounds per square inch (psi) of hydrogen (H_2) gas. The free amine on the N2 of Formula **DD1** can be reacted with DBU in a solvent like dioxane at 100 °C to cyclize to form a C_{6-7} heterocycle fused to Ring C of Formula **DD2**. The cyclized lactam of Formula **DD2** can be treated with a halogen (e.g., R_D= Br)-substituted aromatic of Formula **DD3** with bases such as K_2CO_3, potassium bis(trimethylsilyl)amide (KHMDS) in THF with additional solvents such as ACN and DMF with stirring at 80 °C to afford Formula **DD4**. The BOC

protected amine of Formula **DD4** can be deprotected under acidic conditions such as HCl in solvents like dioxane and DCM to form the amine of Formula **DD5**. The amine of Formula **DD5** can be treated with a halogen (e.g., R_B= F)-substituted aromatic of Formula **AA3** using standard SNAr conditions such as K_3PO_4 in a solvent like *tert*-amyl alcohol and H_2O with stirring at 100 °C to afford Formula **III**. In Formula **III,** when R_1 is an iodine, can react further with an urea with a base like Cs_2CO_3 and palladium catalyst such as ((*SP*-4-3)-[[5-(diphenylphosphino)-9,9-dimethyl-9*H*-xanthen-4-yl]diphenylphosphine-κ*P*](methanesulfonato-κ*O*)[2′-(methylamino-κ*N*)[1,1′-biphenyl]-2-yl-κ*C*]- palladium) XantPhos Pd G4 in a solvent like *tert*-amyl alcohol at 90 °C to form an urea at R_1 in Formula **III**.

In order that this disclosure may be better understood, the following examples are set forth. These examples are for the purpose of illustration only and are not to be construed as limiting the scope of the disclosure in any manner.

Examples

The compounds and intermediates described below were named using the naming convention provided with ChemDraw version 20.1.1.123. The naming convention provided with ChemDraw version 20.1.1.123 is well known by those skilled in the art and it is believed that the naming convention generally comports with the IUPAC (International Union for Pure and Applied Chemistry) recommendations on Nomenclature of Organic Chemistry and the CAS Index rules. Unless noted otherwise, all reactants were obtained commercially without further purifications or were prepared using methods known in the literature.

The following illustrates the synthesis of various compounds of the present invention. Additional compounds within the scope of this invention may be prepared using the methods illustrated in these Examples, either alone or in combination with techniques generally known in the art.

All starting materials in these Preparations and Examples are either commercially available or can be prepared by methods known in the art or as described herein.

Commercial solvents and reagents were generally used without further purification. Anhydrous solvents were employed where appropriate, generally ACROSEAL™ products from Acros Organics, Aldrich SURE/SEAL™ from Sigma- Aldrich, or DRISOLV™ products from EMD Chemicals. Commercial solvents and reagents were used without further purification.

Experiments were generally carried out under inert atmosphere (nitrogen or argon), particularly in cases where oxygen- or moisture-sensitive reagents or intermediates were employed.

Unless otherwise noted, chemical reactions were performed at room temperature (about 23 degrees Celsius).

In some examples, chiral separations were carried out to separate enantiomers or diastereomers of certain compounds of the disclosure.

For syntheses referencing procedures in other Examples or Methods, reaction conditions (reaction time and temperature) may vary. In general, reactions were followed by thin-layer chromatography (TLC) or mass spectrometry (MS) and subjected to work-up when appropriate.

Commercial benchtop photoreactors such as the Penn OC Photoreactor M2, Acceled Photoreactor M2 and Lumidox II with 24-well block were utilized with 450 or 445 nanometer (nm) light-emitting diode (LED).

Purifications may vary between experiments: in general, solvents and the solvent ratios used for eluents/gradients were chosen to provide appropriate retention times.

Reaction progress was monitored using thin layer chromatography (TLC), liquid chromatography-mass spectrometry (LCMS) and high-performance liquid chromatography (HPLC), analyses. TLC was performed on pre-coated silica gel plates with a fluorescence indicator (254 nm excitation wavelength) and visualized under ultraviolet (UV) light.

LCMS data were acquired on an Agilent 1100 Series instrument with a Leap Technologies autosampler, Gemini C_{18} columns, ACN/water gradients, and either trifluoroacetic acid (TFA), formic acid, or ammonium hydroxide (NH_4OH) modifiers or similar equipment. The column eluent was analyzed using Waters ZQ mass spectrometer scanning in both positive and negative ion modes from 100 to 1200 Da. Other similar instruments were also used.

High resolution mass spectrometry (HR/MS) was gathered on Sciex TripleTOF 5600+ with DuoSpray ionization source with the liquid chromatography instrument with an Agilent Technologies, 1200 binary pump, Agilent 1200 autosampler, Agilent 1200 column compartment, and Agilent 1200 diode array detector. The instrument acquisition and data handling were done with Sciex Analyst TF version 1.7.1.

HPLC data were acquired on an Agilent 1100 Series instrument using Gemini, Sunfire, Welch Boltimate™, Welch Xtimate, Prep PG-45 MOD10, Boston Prime, Boston Green ODS, Phenomenex Gemini NX or XBridge C_{18} columns with acetonitrile (ACN)/water (H_2O) gradients, and either TFA, formic acid, NH_4OH, or ammonium bicarbonate (NH_4HCO_3) modifiers and comparable equipment. Purifications were performed by high performance liquid chromatography (HPLC) and medium performance liquid chromatography (MPLC) using Isco CombiFlash Companion, AnaLogix IntelliFlash 280, Biotage SP1, or Biotage Isolera One instruments and pre-packed Isco RediSep or Biotage Snap silica cartridges and the like.

Chiral purifications were performed by chiral supercritical fluid chromatography (SFC) using Berger or Thar instruments and similar instruments with DAICEL CHIRALCEL OD, OJ; DAICEL CHIRALPAK AD, AS, IF; Chiral Technologies OJ-H, AD-H, OD-H, IA, IB; Lux Cellulose 1; Lux Cellulose 3; Pirkle Covalent (R,R) Whelk-O1; CHIRALPAK IH; YMC-IB; and Phenomenex Lux Cellulose 1 columns; and carbon dioxide (CO_2) mixtures with methanol (MeOH), ethanol (EtOH), isopropyl alcohol, or ACN, alone or modified using TFA, formic acid,

NH_4OH, diethylamine (DEA), ammonia (NH_3) or isopropylamine. UV detection was used to trigger fraction collection.

The chiral purity was determined using supercritical fluid chromatography (SFC) and reverse-phase liquid chromatography (RPLC) analytical method with Chiralpak AD-3, IG-3, IF, AS-3, IB-N; Chiralcel OJ-, OD-3; Chiral Technologies OJ-H, AD-H, OD-H, IA, IB, IH; Lux Cellulose 1; IM-3; Lux Cellulose 3; Phenomenex Kinetex and Regis (R,R) Whelk-01 columns; and CO_2 mixtures with MeOH, EtOH, isopropyl alcohol, or ACN, alone or modified using TFA, formic acid, NH_4OH, DEA, NH_3, or isopropylamine.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded, referenced to residual peaks from the deuterated solvents employed, where δ is chemical shift; d is doublet; dd is doublet of doublets; ddd is doublet of doublet of doublets; dt is doublet of triplets, m is multiplet, s is singlet, t is triplet, q, quartet; quin, quintet, br s, broad singlet; MHz is megahertz, ppm is parts per million. Proton nuclear magnetic spectroscopy (^{1}H NMR) chemical shifts are given in parts per million (ppm, δ) referenced to the deuterated solvent downfield from tetramethylsilane and were recorded on 300, 400, 500, or 600 MHz Varian spectrometers.

Products were generally dried under vacuum before being carried on to further reactions or submitted for biological testing.

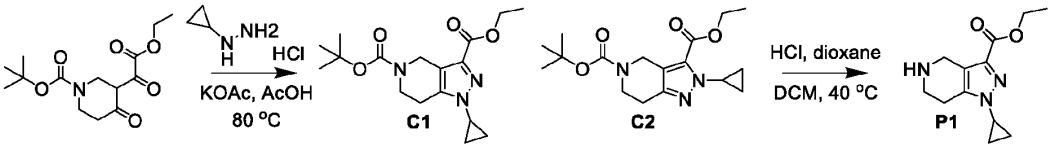
In the experimental sections that follow the following abbreviations may be used. ACN is acetonitrile; abs in the structures is absolute and refers to the stereochemistry being confirmed as R or S; AcOH is acetic acid; APhos Pd G3 is [4-(di-*tert*-butylphosphino)-*N,N*-dimethylaniline-2-(2′-aminobiphenyl)]palladium(II) methanesulfonate; BBr_3 is boron tribromide; B_2Pin_2 is bis(pinacolato)diboron; BOC is *tert*-butyloxycarbonyl; Boc_2O is di-*tert*-butyl dicarbonate; brine is a saturated sodium chloride water solution; BINAP is (±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene; BF_3OEt_2 is boron trifluoride diethyl etherate; °C is degrees Celsius; $CDCl_3$ is deuterated chloroform; CD_3OD is deuterated methanol; $(CD_3)_2SO$ is deuterated dimethyl sulfoxide; cataCXium® A is di(1-adamantyl)-*n*-butylphosphine; cataCXium® A Pd G3 is mesylate[(di(1-adamantyl)-n-butylphosphine)-2-(2′-amino-1,1′-biphenyl)]palladium(II); CAS is Chemical Abstracts Service; CDI is 1,1′-carbonyldiimidazole; $CHCl_3$ is chloroform; CO_2 is carbon dioxide; $CsHCO_3$ is cesium hydrogencarbonate; Cs_2CO_3 is cesium carbonate; CsF is cesium fluoride; CuI is copper(I) iodide; DBU is 1,8-diazabicyclo[5.4.0]undec-7-ene; DCM is dichloromethane; DCE is 1,2-dichloroethane; DDQ is 2,3-dichloro-5,6-dicyano-*p*-benzoquinone; DEA is diethylamine; DIEA is *N,N*-diisopropylethylamine; dioxane is 1,4-dioxane; DMA is dimethylacetamide; DMAP is 4-(dimethylamino)pyridine; DME is dimethyl ether; DMEDA is 1,2-dimethylethylenediamine; DMF is *N,N*-dimethylformamide; DMSO is dimethyl sulfoxide; EDCI is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride; ee is enantiomeric excess; EtOAc is ethyl acetate; EtOH is ethanol; g is gram; g/L is grams per liter; h is hour; HATU is 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate; HCl is hydrochloric acid; H_2 is hydrogen; H_2O is water; HOBt is 1-hydroxybenzotriazole hydrate;

HOPO is 2-pyridinol 1-oxide; HPLC is high performance liquid chromatography; HR/MS is high resolution mass spectrometry; Hz is hertz; $Ir(ppy)_2(dtbbpy)PF_6$ is [4,4′-b*is*(1,1-dimethylethyl)-2,2′-bipyridine-*N*1,*N*1′]*bis*[2-(2-pyridinyl-*N*)phenyl-C]iridium(III) hexafluorophosphate; $KHSO_4$ is potassium bisulfate; KHMDS is potassium bis(trimethylsilyl)amide; KOAc is potassium acetate; KOH is potassium hydroxide; KOTMS is potassium trimethylsilanolate; K_2CO_3 is potassium carbonate; kg is kilogram; K_3PO_4 is tripotassium phosphate; KH_2PO_4 is potassium phosphate monobasic; L is liter; LC is liquid chromatography; LCMS is liquid chromatography mass spectrometry; LDA is lithium diisopropylamide; LED is light-emitting diode; LiOH is lithium hydroxide monohydrate; M is molar; LiHMDS is lithium bis(trimethylsilyl)amide; MeI is iodomethane; MeOH is methanol; 4Me*t*BuXPhos Pd G3 is methanesulfonato (2-di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2′,4′,6′-triisopropyl-1,1-biphenyl)(2′-amino-1,1′-biphenyl-2-yl) palladium(II); mg is milligram; $MgSO_4$ is magnesium sulfate; MPLC is medium performance liquid chromatography; MHz is megahertz; min is minute; mL is milliliter; mL/min is milliliter per minute; mmol is millimole; mol is mole; mM is millimolar; mm is millimeter; MPa is megapascal; MS is mass spectrometry; MTBE is methyl tertiary-butyl ether; m/z is mass-to-charge ratio; N is normal (concentration); N_2 is nitrogen; NBS is *N*-bromosuccinimide; $NaBH_4$ is sodium borohydride; ND is not determined; *N*-XantPhos Pd G3 is (2′-amino-2-biphenylyl)(methanesulfonato-κ*O*)palladium - 4,6-bis(diphenylphosphino)-10*H*-phenoxazine; NH_3 is ammonia; Na_2CO_3 is sodium carbonate; NaH is sodium hydride; $NaHCO_3$ is sodium bicarbonate; NaI is sodium iodide; $NaOCH_3$ is sodium methoxide; NaOH is sodium hydroxide; Na_2SO_4 is sodium sulfate; NaOtBu is sodium *tert*-butoxide; *n*-BuLi is *n*-butyllithium; NH_4Cl is ammonium chloride; NH_4HCO_3 is ammonium bicarbonate; NH_4OH is ammonium hydroxide; NMR is nuclear magnetic resonance; $NiCl_2$.glyme is nickel(II) chloride ethylene glycol dimethyl ether complex; $NiBr_2$.DME is nickel(II) bromide ethylene glycol dimethyl ether complex; P(*t*-Bu)$_3$ Pd G2 is chloro[(tri-*tert*-butylphosphine)-2-(2-aminobiphenyl)] palladium(II); $Pd(dppf)Cl_2$ is (1,1'-bis(diphenylphosphino)ferrocene)palladium(II) dichloride; Pd/C is palladium on carbon; $Pd_2(dba)_3$ is tris(dibenzylideneacetone)dipalladium(0); $PdCl_2(PPh_3)_2$ is bis(triphenylphosphine)palladium(II) dichloride; $Pd(OAc)_2$ is palladium(II) acetate; Pd(*t*-$Bu_3P)_2$ is bis(tri-*tert*-butylphosphine)palladium(0); PE is petroleum ether; psi is pounds per square inch; quinuclidine is 1-azabicyclo[2.2.2]octane; SFC is super critical fluid chromatography; $SOCl_2$ is thionyl chloride; TBD is 1,5,7-triazabicyclo[4.4.0]dec-5-ene; TEA is triethylamine; *tert*-amyl alcohol is 2-methyl-2-butanol; TFA is trifluoroacetic acid; THF is tetrahydrofuran; TLC is thin-layer chromatography; trimethylboroxine is 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane; µm is micrometer; µmol is micromole; *rac* is racemic referring to the compound including a mixture of compounds having both R and S stereochemistry and is denoted in the structures as "&1"; *rel* is relative referring to the stereochemistry being either R or S and is denoted in the structures as "or1" or as an asterisk in the named structure if there are two chiral centers in the compound; $RhCl(PPh_3)_3$ is tris(triphenylphosphine)rhodium(I) chloride; rpm is revolutions per minute; RPLC

is reverse-phase liquid chromatography; Ru/Al_2O_3 is ruthenium on aluminum oxide; RuPhos is 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl; RuPhos Pd G3 is (2-dicyclohexylphosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate; RuPhos Pd G4 is [dicyclohexyl(2′,6′-diisopropoxy-2-biphenylyl)phosphine-κ*P*](methanesulfonatato-κ*O*)[2′-(methylamino-κ*N*)-2-biphenylyl-κ*C*^{2}]palladium; $RuCl(PPh_3)_3$ Ru/SiO_2 is ruthenium on silica; wt is weight; XPhos Pd G2 is chloro(2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II); XantPhos Pd G4 is (*SP*-4-3)-[[5-(diphenylphosphino)-9,9-dimethyl-9*H*-xanthen-4-yl]diphenylphosphine-κ*P*](methanesulfonato-κ*O*)[2′-(methylamino-κ*N*)[1,1′-biphenyl]-2-yl-κ*C*]- palladium; and Zn is zinc.

Preparation 1

Ethyl 1-cyclopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P1**)



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-cyclopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C1**) and 5-(*tert*-butyl) 3-ethyl 2-cyclopropyl-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C2**)

A reaction containing cyclopropylhydrazine monohydrochloride (36.3 mg, 0.334 mmol) and KOAc (36.1 mg, 0.367 mmol) in AcOH (1.0 mL) was heated at 80 °C for 10 min then cooled to room temperature. *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 0.100 g, 0.334 mmol) was added to the mixture. The reaction turned into a viscous yellow oil, which was stirred at 80 °C for 1 h and 30 min. The reaction was then diluted with EtOAc and saturated aqueous $NaHCO_3$. The organic layer was separated and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-40% EtOAc: heptane) to provide minor first eluting isomer **C2**: (11 mg, 27.2% yield) (LC/MS) m/z $(M+H)^+$ = 336.3; followed by major second eluting isomer **C1**: (18 mg, 44.5% yield) (LC/MS) m/z $(M+H)^+$ = 336.3; ^1H NMR (600 MHz, $CDCl_3$) δ 4.66- 4.54 (m, 2H), 4.36 (q, 2H), 3.71 (s, 2H), 3.40- 3.34 (m, 1H), 2.84- 2.74 (m, 2H), 1.48-1.43 (m, 9H), 1.41- 1.34 (m, 3H), 1.21- 1.18 (m, 2H), 1.07- 1.02 (m, 2H).

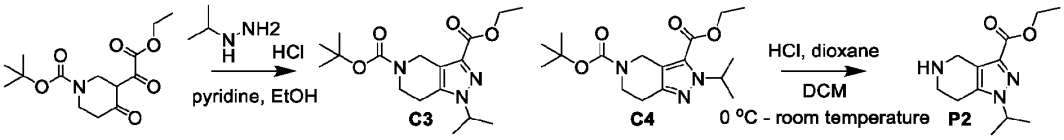
Step 2. Preparation of ethyl 1-cyclopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P1**)

A solution of **C1** (0.200 g, 0.596 mmol) was dissolved in DCM (2.0 mL), then 4M HCl in dioxane (0.130 g, 3.58 mmol) was added, then the reaction was stirred at 40 °C for 25 min. The

reaction was concentrated *in vacuo* to provide **P1** (0.168 mg, crude) as a white solid. The solid was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 236.2; ^{1}H NMR (600 MHz, CD_3OD) δ 4.41– 4.33 (m, 4H), 3.61- 3.53 (m, 3H), 3.16 (t, 2H), 1.37 (t, 3H), 1.21 – 1.16 (m, 2H), 1.15 – 1.09 (m, 2H).

Preparation 2

Ethyl 1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P2**)



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-isopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C3**) and 5-(*tert*-butyl) 3-ethyl 2-isopropyl-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C4**)

To a solution of *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4, 325 g, 1.09 mol) in EtOH (2.3 L) was added isopropylhydrazine hydrochloride (120 g, 1.1 mol) in one portion then pyridine (103 g, 1.30 mol) was added dropwise into the mixture for 10 min at 20- 25 °C with ice water bath. The reaction mixture was stirred for 2 h at room temperature. The reaction was carried out in two batches in parallel, were combined, and then concentrated *in vacuo*. The residue was diluted with EtOAc (5 L) and washed with brine (2 x 5 L) then dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc: PE from 10-50%) to provide **C3** and **C4**. **C3** was dissolved in PE (0.8 L) and then cooled to -20 °C. The mixture was stirred for 4 h, resulting solids were filtered, and washed with PE (0.1 L). The filter cake was dried under high vacuum to obtain **C3** (414 g, 55.9% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 338.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.59 (s, 2H), 4.48- 4.32 (m, 3H), 3.71 (t, 2H), 2.70 (t, 2H), 1.53 – 1.45 (m, 15H), 1.39-1.34 (m, 3H). **C4** was dissolved in PE (50 mL) then cooled to -20 °C. The mixture was stirred for 4 h, resulting solids were filtered, and washed with PE (20 mL). The filter cake was dried under high vacuum to provide **C4** (11.7 g, 1.58% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 338.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60- 5.43 (m, 1H), 4.60 (s, 2H), 4.33 (q, 2H), 3.68 (s, 2H), 2.75 (s, 2H), 1.50- 1.44 (m, 15H), 1.38 (m, 3H).

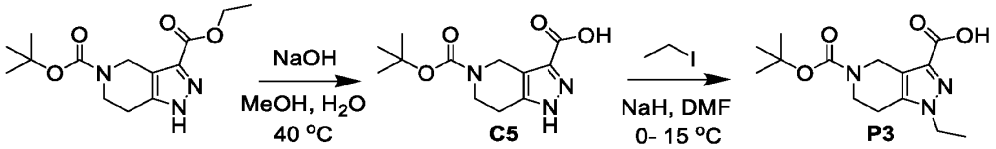
Step 2. Preparation of ethyl 1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P2**)

To a mixture of **C3** (13.5 g, 40.0 mmol) in DCM (60 mL) was added 4N HCl in dioxane (150 mL) in batches at 0 °C. The reaction was stirred at about 15 °C for 16 h and then concentrated *in vacuo* to provide **P2** (10.5 g, crude) as a white solid, used directly in the next step without further purification. LC/MS m/z $(M+H)^+$ = 238.1; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ

9.80 (s, 1H), 4.63- 4.51 (m, 1H), 4.28 (q, 2H), 4.18 (s, 2H), 3.36 (s, 2H), 3.02 (t, 2H), 1.38 (d, 6H), 1.29 (t, 3H).

Preparation 3

5-(*tert*-Butoxycarbonyl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**P3**)



Step 1. Preparation of 5-(*tert*-butoxycarbonyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C5**)

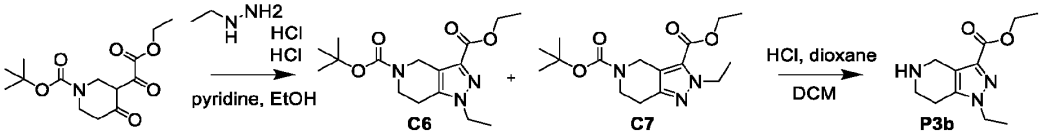
To a suspension of 5-(*tert*-butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 2.00 g, 6.77 mmol) in MeOH (7.7 mL) and H_2O (7.7 mL) was added NaOH (0.542 g, 13.5 mmol). The reaction mixture was stirred at 40 °C for 16 h. The mixture was diluted with H_2O (20 mL), cooled to 0 °C and acidified with 1M aqueous HCl to pH of about 3. The resulting mixture was filtered, the solid was dried further under a high vacuum and then lyophilized to provide **C5** (1.60 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 268.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 13.17 (br s, 2H), 4.48 (s, 2H), 3.58 (t, 2H), 2.65 (t, 2H), 1.41 (s, 9H).

Step 2. Preparation of 5-(*tert*-butoxycarbonyl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**P3**)

To the suspension of **C5** (0.200 g, 0.748 mmol) in DMF (3.5 mL) was added NaH (89.8 mg, 2.24 mmol, 60%) at 0 °C and stirred for 30 min at 0 °C. A solution of iodoethane (0.140 g, 0.898 mmol) in DMF (0.5 mL) was added at 0 °C then stirred at 15 °C for about 4 h. An additional portion of the solution of iodoethane (23.3 mg, 0.150 mmol) in DMF (0.2 mL) was added to the mixture and stirred at 15 °C for 16 h. The reaction solution was quenched with H_2O (10 mL) and then extracted with EtOAc (2 x 20 mL). The aqueous layer was acidified with 1M aqueous HCl to pH ~3 and then extracted with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (2 x 30 mL), dried over Na_2SO_4, concentrated *in vacuo* and then lyophilized to provide **P3** (0.173 g, 78.5% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 296.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.64 (br s, 1H), 4.45 (s, 2H), 4.07 (q, 2H), 3.60 (t, 2H), 2.74-2.65 (m, 2H), 1.41 (s, 9H), 1.31 (t, 3H).

Preparation 3b

Ethyl 1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P3b)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-ethyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C6)** and 5-(*tert*-butyl) 3-ethyl 2-ethyl-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C7)**

To a solution of *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 97.5 g, 326 mmol) and ethylhydrazine dihydrochloride (56.3 g, 423 mmol) in EtOH (1.6 L) was added pyridine (129 g, 1.63 mol). The reaction mixture was stirred at room temperature for 16 h then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-50% THF: PE) to provide the first eluting isomer **C6** (58.0 g) as a white solid; followed by the second eluting isomer **C7** (20.6 g, 19.6% yield) as a light-yellow oil. **C6** was diluted with EtOAc (200 mL) then stirred at 50 °C for 30 min and cooled to 0 °C which caused white solid precipitate to form. The suspension was filtered, and the filter cake was washed with EtOAc (3 x 10 mL). The filter cake was collected and concentrated *in vacuo* to provide **C6** (35.4 g, 33.6% yield) as a white solid.

C6: (LC/MS) m/z $(M+H)^+$ = 324.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.60 (s, 2H), 4.38 (q, 2H), 4.12 (q, 2H), 3.71 (t, 2H), 2.68 (t, 2H), 1.47 (s, 9H), 1.44 – 1.34 (m, 6H).

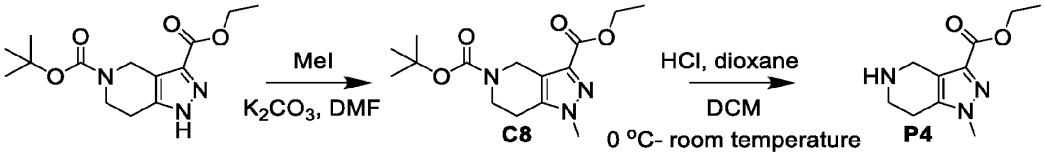
C7: (LC/MS) m/z $(M+H)^+$ = 324.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 – 4.50 (m, 4H), 4.34 (q, 2H), 3.73 – 3.63 (m, 2H), 2.80 – 2.67 (m, 2H), 1.48 (s, 9H), 1.43 – 1.33 (m, 6H).

Step 2. Preparation of ethyl 1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P3b)**

To a solution of **C6** (1.00 g, 3.09 mmol) in DCM (10 mL) was added 2M HCl in dioxane (1.13 g, 30.9 mmol). The reaction mixture was stirred at room temperature for 2.5 h then concentrated *in vacuo* to provide **P3b** (0.870 g, crude) as a white solid. The solid was used directly in the nest step without further purification. (LC/MS) m/z $(M+H)^+$ = 224.2. ^{1}H NMR (400 MHz, CD_3OD) δ 4.44 – 4.32 (m, 4H), 4.20 (q, 2H), 3.56 (t, 2H), 3.09 (t, 2H), 2.80 – 2.67 (m, 2H), 1.44 (t, 3H), 1.38 (t, 3H).

Preparation 4

Ethyl 1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P4**)



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C8**)

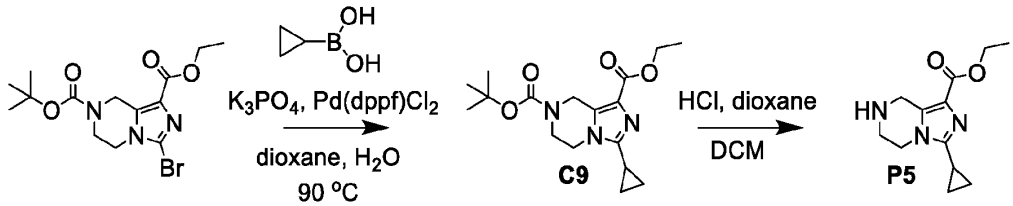
5-(*tert*-Butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 2.00 g, 6.77 mmol) was dissolved in DMF (10.0 mL) then K_2CO_3 (2.81 g, 20.3 mmol) and MeI (0.961 g, 6.77 mmol) were added. The reaction was stirred at room temperature for 3 h and diluted with EtOAc and H_2O. The organic layer was separated and then concentrated *in vacuo*. The residue was dissolved in DCM and then purified by column chromatography (silica gel, 0-40% EtOAc: heptane) to provide **C8** (0.825 g, 39.4% yield) as a clear oil. (LC/MS) m/z $(M+H)^+$ = 310.3; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.61 (s, 2H), 4.35 (q, 2H), 4.14 (s, 3H), 3.68 (s, 2H), 2.74 (s, 2H), 1.49 (s, 9H), 1.41- 1.37 (m, 3H).

Step 2. Preparation of ethyl 1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P4**)

C8 (2.00 g, 6.46 mmol) was dissolved in 4M HCl in dioxane (40.0 mL) at 0 °C and then stirred at room temperature for 16 h. The reaction was concentrated *in vacuo* to provide **P4** (1.30 g, 81.9% yield) as a yellow solid. This was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 210.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (br s, 1H), 4.50 – 4.32 (m, 4H), 3.86 (s, 3H), 3.55- 3.46 (m, 2H), 3.13 (t, 2H), 1.40 (t, 3H).

Preparation 5

Ethyl 3-cyclopropyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride (**P5**)



Step 1: Preparation of 7-(*tert*-butyl) 1-ethyl 3-cyclopropyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (**C9**)

To a solution of 7-(*tert*-butyl) 1-ethyl 3-bromo-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (CAS: 2108354-93-2; 0.578 g, 1.54 mmol) and cyclopropylboronic acid (CAS: 411235-57-9, 0.398 g, 4.63 mmol) in dioxane (8.0 mL) and H_2O (1.0 mL) was added K_3PO_4 (0.984 g, 4.63 mmol) and $Pd(dppf)Cl_2$ (0.226 g, 0.309 mmol) at room temperature under

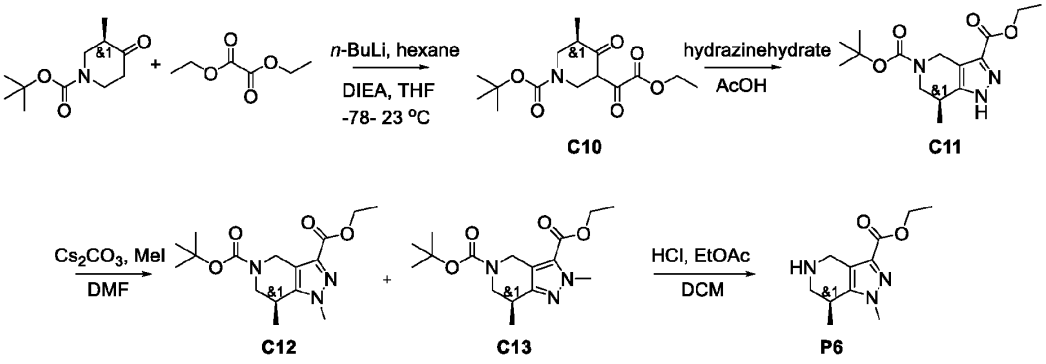
nitrogen gas. The reaction was stirred at 90 °C for 16 h. The resulting solution was concentrated *in vacuo* to give a solid that was purified by column chromatography (silica gel, 0-95% EtOAc: PE) to provide **C9** (0.400 g, 77.2% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 336.1. ^{1}H NMR (400 MHz, CD_3OD) δ 4.84 (s, 2H), 4.30 (q, 2H), 4.14 – 4.04 (m, 2H), 3.86 (t, 2H), 1.94- 1.86 (m, 1H), 1.53- 1.48 (m, 9H), 1.36 (t, 3H), 1.00- 0.96 (m, 4H).

Step 2. Preparation of ethyl 3-cyclopropyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride (**P5**)

To a solution of **C9** (0.300 g, 0.894 mmol) in DCM (5.0 mL) was added 2M HCl in dioxane (0.261 g, 7.16 mmol) and reaction stirred at room temperature for 16 h. The resulting suspension was concentrated *in vacuo* to provide **P5** (0.243 g, crude) as a white solid, used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.17 (s, 1H), 4.50 (s, 2H), 4.36 (t, 2H), 4.25 (q, 2H), 3.62- 3.57 (m, 2H), 2.13- 2.03 (m, 1H), 1.30-1.23 (m, 3H), 1.04 – 0.98 (m, 2H), 0.97 – 0.91 (m, 2H).

Preparation 6

rac-Ethyl (*R*)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P6**)



Step 1: Preparation of *rac*-tert-butyl (5*R*)-3-(2-ethoxy-2-oxoacetyl)-5-methyl-4-oxopiperidine-1-carboxylate (**C10**)

A solution of diisopropylamine (4.2 g, 41 mmol) in THF (19.0 mL) was cooled to –78 °C before 2.5M *n*-BuLi in hexane (2.5 g, 39 mmol) was added. After the addition, the reaction mixture was warmed to 0 °C and stirred for 15 min. The reaction was then cooled to –78 °C and a solution of *rac-tert*-butyl (*R*)-3-methyl-4-oxopiperidine-1-carboxylate (CAS:181269-69-2, 7.0 g, 33 mmol) in THF (81.0 mL) was slowly added while maintaining the temperature below -67 °C. The mixture was stirred at -78 °C for about 1 h and 30 min before diethyl oxalate (4.8 g, 33 mmol) was added to the reaction solution. The resulting mixture was allowed to warm to room temperature and then stirred for 2 h. The mixture was neutralized with 1N HCl (80 mL) and extracted with EtOAc (2 x 200 mL). The combined organic layers were washed with brine (400

mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-10% EtOAc: PE) to provide **C10** (4.8 g, 47% yield) as a yellow oil. (LC/MS) m/z $(M+H)^+$ = 314.4. ^1H NMR (400 MHz, $CDCl_3$) δ 4.51 – 4.30 (m, 3H), 3.91 – 3.65 (m, 1H), 3.34 – 3.12 (m, 1H), 2.76 – 2.60 (m, 1H), 1.51 – 1.44 (m, 9H), 1.41 – 1.34 (m, 3H), 1.28 – 1.20 (m, 3H).

Step 2: Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C11**)

To a solution of **C10** (3.55 g, 11.3 mmol) in AcOH (14.2 mL), hydrazine hydrate was added (2.09 g, 65% wt, 27.2 mmol). During the addition, the reaction mixture became exothermic to 65 °C. The reaction mixture was stirred for 1 h then concentrated *in vacuo*. The residue was diluted with H_2O followed by saturated aqueous $NaHCO_3$ (200 mL). The mixture was extracted with EtOAc (2 x 200 mL). The combined organic layers were dried with Na_2SO_4, filtered, concentrated *in vacuo*, and dried further under a high vacuum to provide **C11** (3.45 g, crude) as a pale-yellow solid, used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 310.40.

Step 3: Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1,7-dimethyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C12**) and *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-2,7-dimethyl-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C13**)

To a solution of **C11** (3.45 g, 11.2 mmol) in DMF (28.6 mL), Cs_2CO_3 (3.65 g, 11.2 mmol) was added, followed by MeI (4.80 g, 33.5 mmol). The reaction mixture was stirred for 16 h at room temperature, diluted with H_2O (100 mL) and extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with saturated aqueous NH_4Cl (2 x 100 mL) and H_2O (2 x 100 mL). The organic layer was dried over Na_2SO_4, filtered, and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 10-100% EtOAc: heptane) to provide **C13** (2.12 g, 58.9% yield) and **C12** (0.999 g, 27.7% yield).

C13: (LC/MS) m/z $(M+H)^+$ = 324.1. ^1H NMR (400 MHz, $CDCl_3$) δ 4.74 – 4.41 (m, 2H), 4.38 – 4.27 (m, 2H), 4.17 – 4.10 (m, 3H), 3.98 – 3.65 (m, 1H), 3.36 – 2.88 (m, 2H), 1.48 (s, 9H), 1.38 (t, *3*H), 1.26 (d, *3*H).

C12: (LC/MS) m/z $(M+H)^+$ = 324.1. ^1H NMR (400 MHz, $CDCl_3$) δ 5.18 – 4.87 (m, 1H), 4.43 – 4.30 (m, 2H), 4.27 – 3.99 (m, 2H), 3.85 (s, 3H), 3.23 – 2.87 (m, 2H), 1.51 – 1.43 (m, 9H), 1.41 – 1.33 (m, 3H), 1.24 (d, 3H).

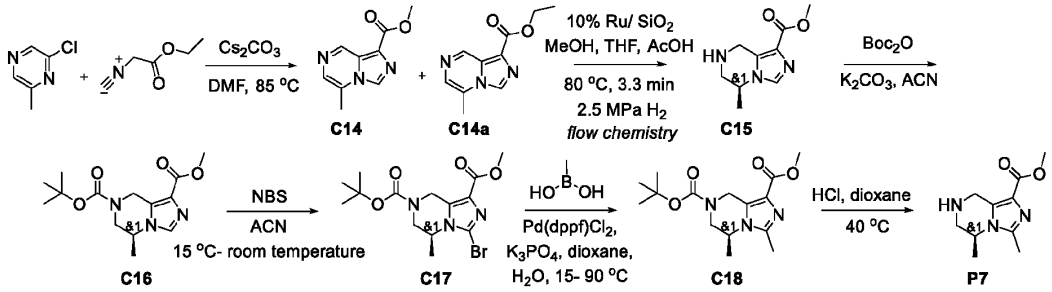
Step 4: Preparation of *rac*-ethyl (*R*)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (**P6**)

To a solution of **C12** (0.536 g, 1.66 mmol) in DCM (9.7 mL) was added 1M HCl in EtOAc (5.0 mL) at room temperature. The reaction was stirred at room temperature for 16 h. An additional portion of 1M HCl in EtOAc (5.0 mL) was added at room temperature then stirred for

1 h. The reaction was concentrated *in vacuo* to provide **P6** (0.426 g, 99.1% yield) as an off-white solid. This was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 224.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.58 – 10.31 (m, 1H), 10.18 – 9.87 (m, 1H), 4.58 – 4.49 (m, 1H), 4.46 – 4.32 (m, 3H), 3.92 (s, 3H), 3.51 – 3.25 (m, 3H), 1.57 – 1.53 (m, 3H), 1.40 (t, 3H).

Preparation 7

rac-Methyl (*R*)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride (**P7**)



Step 1. Preparation of methyl 5-methylimidazo[1,5-*a*]pyrazine-1-carboxylate (**C14**) and ethyl 5-methylimidazo[1,5-*a*]pyrazine-1-carboxylate **(C14a)**

To a mixture of 2-chloro-6-methylpyrazine (CAS: 38557-71-0, 15.0 g, 117 mmol) in DMF (150.0 mL) was added Cs_2CO_3 (57.0 g, 175 mmol) and ethyl 2-isocyanoacetate (CAS: 2999-46-4, 26.6 g, 233 mmol). The reaction was heated to 85 °C and stirred for 16 h. The light brown reaction mixture was filtered then the solid was washed with MeOH. The filtrate was concentrated *in vacuo*. The brown residue was purified by column chromatography (silica gel, 0-100% EtOAC: PE then 2% MeOH: EtOAc). Transesterification occurred during workup and purification to generate **C14** (9.50 g, 42.6% yield) as a light brown solid (LC/MS) m/z $(M+H)^+$ = 192.1 and a mixture of (2:1, **C14a:C14**) (1.1 g, 4.59% yield) (LC/MS) m/z $(M+H)^+$ = 206.1. **C14** was brought forward to the next step.

C14: ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.32 (s, 1H), 8.68 (s, 1H), 7.74 (s, 1H), 3.90 (s, 3H), 2.63 (s, 3H).

Step 2. Preparation of *rac*-methyl (*R*)-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate (**C15**)

The reaction was carried out via flow chemistry. **C14** (2.90 g, 15.2 mmol) was suspended in MeOH (50.0 mL), THF (50.0 mL) and AcOH (0.6 mL) then heated to 50 °C to dissolve to a solution. The solution was pumped with a flow rate of 0.3 mL/min and the H_2 had a rate of 30 mL/ min. The solution passed through the fixed bed (6.350 (1/4") mm) packed with granular catalyst 10% Ru/SiO_2 (15.3 g, 1.52 mmol) with a 5.0 mL volume and was hydrogenated for 3.3 min at 80 °C via flow at 2.5 MPa H_2. The light-yellow reaction was

concentrated *in vacuo* then dried in high vacuum to provide **C15** (2.96 g, crude) as a light brown oil. This was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 4.43 (d, 1H), 4.27 – 4.15 (m, 2H), 3.87 (s, 3H), 3.32 (dd, 1H), 2.84 (dd, 1H), 2.68 (s, 1H), 1.53 (d, 3H).

Step 3. Preparation of *rac*-7-(*tert*-butyl) 1-methyl (*R*)-5-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (**C16**)

To a solution of **C15** (2.96 g, 15.2 mmol) in ACN (60.0 mL) was added Boc_2O (4.97 g, 22.8 mmol) and K_2CO_3 (6.29 g, 45.5 mmol) at room temperature. The reaction was stirred at room temperature for 16 h. The light brown reaction mixture was filtered then concentrated *in vacuo.* The brown residue was purified by column chromatography (silica gel; 0-100% EtOAc: PE) to provide **C16** (3.02 g, 67.5% yield) as an off-white solid. (LC/MS) m/z $(M+H)^+$ = 296.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 5.01 – 4.77 (m, 2H), 4.33 – 4.21 (m, 1H), 3.89 (s, 3H), 3.55 – 3.34 (m, 2H), 1.53 – 1.49 (m, 12H).

Step 4. Preparation of *rac*-7-(*tert*-butyl) 1-methyl (*R*)-3-bromo-5-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (**C17**)

To a solution of **C16** (3.02 g, 10.2 mmol) in ACN (50.0 mL) was added NBS (2.73 g, 15.4 mmol) at 15 °C. The reaction was stirred at room temperature for 16 h. The light brown reaction mixture was concentrated *in vacuo.* The brown residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE) which gave an impure **C17** as a light brown solid. The solid was triturated with EtOAc: PE (1:5). The solid was filtered then rinsed with EtOAc: PE (5:1) to provide **C17** (1.32 g, 34.4% yield) as a white solid. (LC/MS) m/z $(M+2H)^+$ = 376.0. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 – 5.23 (m, 1H), 4.54 – 4.22 (m, 3H), 3.93 – 3.86 (m, 3H), 3.48 – 3.16 (m, 1H), 1.51 (s, 9H), 1.43 (d, 3H).

Step 5. Preparation of *rac*-7-(*tert*-butyl) 1-methyl (*R*)-3,5-dimethyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (**C18**)

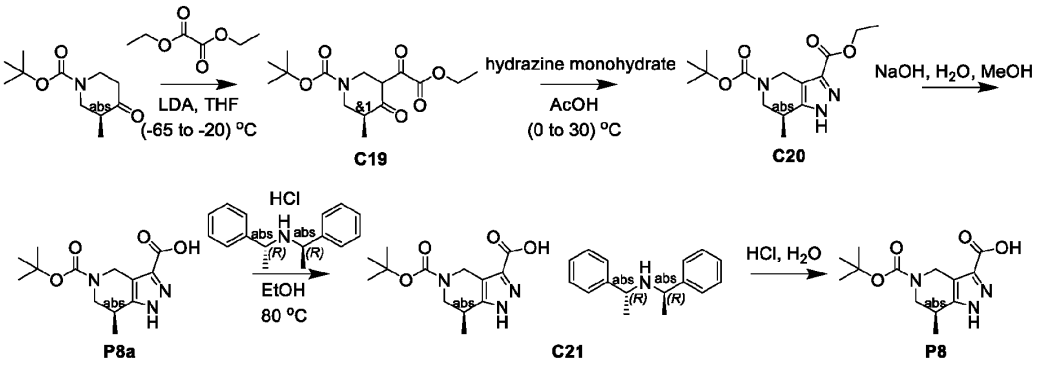
To a solution of **C17** (1.30 g, 3.47 mmol) and methylboronic acid (0.624 g, 10.4 mmol) in dioxane (28.0 mL) and H_2O (7.0 mL) was added K_3PO_4 (2.21 g, 10.4 mmol) then $Pd(dppf)Cl_2$ (0.519 g, 0.695 mmol) at 15 °C under nitrogen. The reaction was heated to 90 °C for 16 h. The brown reaction mixture was extracted with EtOAc (30 mL). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo.* The brown residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE then 2% MeOH: EtOAc) then dried by high vacuum to provide **C18** (0.460 g, 42.8%) as a light brown solid. (LC/MS) m/z $(M+H)^+$ = 310.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51 – 5.15 (m, 1H), 4.52 – 4.14 (m, 3H), 3.87 (s, 3H), 3.32 - 3.10 (m, 1H), 2.39 (s, 3H), 1.50 (s, 9H), 1.36 (d, 3H).

Step 6. Preparation of *rac*-methyl (*R*)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride (**P7**)

To a solution of **C18** (140 mg, 0.452 mmol) in DCM (4.0 mL) was added 2M HCl in dioxane (8.0 mL) at room temperature. The reaction was heated to 40 °C and stirred for 2 to 5 h. The light brown reaction mixture was concentrated *in vacuo* and dried further under high vacuum to provide **P7** (0.111 g, crude) as a light brown solid. The solid was used in the next step without further purification.

Preparation 8

(*S*)-5-(t*ert*-Butoxycarbonyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(P8)**



Step 1. Preparation of *rac-tert*-butyl (5*S*)-3-(2-ethoxy-2-oxoacetyl)-5-methyl-4-oxopiperidine-1-carboxylate **(C19)**

Under a nitrogen balloon at -65 °C, LDA (44.4 g, 0.414 mol, 207 mL) was added to THF (350 mL) then a solution of *tert*-butyl (*S*)-3-methyl-4-oxopiperidine-1-carboxylate (CAS: 2092486-33-2; 88.4 g, 0.414 mol) in THF (350 mL) was added dropwise over 1 h to keep the inner temperature below -65 °C. The reaction mixture was stirred at -65 °C for 1 h before a solution of diethyl oxalate (CAS: 95-92-1; 60.6 g, 0.414 mol) in THF (350 mL) was added dropwise at -65 °C. After the addition, the reaction mixture was stirred at -65°C for 1 h, then warmed to -20 °C and stirred for 40 min. At 0 °C under nitrogen gas, the reaction mixture was quenched with 1M aqueous $KHSO_4$ solution (1415 mL), which caused a white precipitate to form. The suspension was filtered, and then the filtrate was extracted with EtOAc (3 x 800 mL). The combined organic layer was washed with brine (800 mL), dried over Na_2SO_4, filtered then concentrated *in vacuo* to provide **C19** (129 g, crude) as a yellow oil. The oil was used directly in the next step without further purification. (LCMS) *m/z* (M-*tert*-butyl group)$^+$ = 257.9. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.21 (br s, 1H), 4.47 – 4.17 (m, 3H), 4.06 – 3.47 (m, 2H), 3.29 – 3.17 (m, 1H), 2.59 - 2.53 (m, 1H), 1.45 – 1.37 (m, 9H), 1.28 – 1.21 (m, 3H), 1.18 – 0.95 (m, 3H).

Step 2. Preparation of enriched 5-(*tert*-butyl) 3-ethyl (*S*)-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C20)**

At 0 °C, to a suspension of **C19** (139 g, 0.443 mol) in AcOH (552 mL) was added hydrazine monohydrate (62.7 g, 1.06 mol) which caused the internal temperature to increase to ~30 °C. The reaction mixture was stirred at room temperature under nitrogen gas for 1 h then was diluted with H_2O (500 mL) and saturated $NaHCO_3$ (1000 mL). The diluted suspension was extracted with EtOAc (2 x 800 mL). The combined organic layer was dried over Na_2SO_4, filtered then concentrated *in vacuo* to give a yellow gum. The gum was purified by column chromatography (silica gel, (1:1) EtOAc: PE) to give the enriched *S*-enantiomer **C20** (123 g, 89.7% yield) as a yellow gum. (LCMS) *m/z* $(M+H)^+$ = 310.0. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 13.71 – 13.28 (m, 1H), 4.63 – 4.18 (m, 4H), 3.86 - 3.59 (m, 1H), 3.12 – 2.80 (m, 2H), 1.40 – 1.38 (m, 9H), 1.30 – 1.24 (m, 3H), 1.17 – 1.13 (m, 3H). The chiral purity was determined using SFC analytical method on Chiralpak AD-3 100 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2 / Mobile phase B: EtOH with 0.2% of NH_3; gradient: 5-40% of Mobile Phase B over 3 min then held at 5% of Mobile phase B for 1 min; backpressure: 1500 psi; flow rate: 2.8 mL/min; column temperature: 35 °C to provide **C20**: major peak ((SFC-MS) *m/z* (M-*tert*-butyl group)$^+$ = 254.04 at retention time: 2.218 min, 94% ee).

Step 3. Preparation of enriched (*S*)-5-(*tert*-butoxycarbonyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(P8a)**

To a solution of **C20** (124 g, 0.400 mol) in MeOH (452 mL) and H_2O (452 mL) was added NaOH (32.0 g, 0.800 mol) then stirred at room temperature for 24 h. The reaction mixture was diluted with H_2O (200 mL) then cooled to 0 °C before the diluted reaction was acidified to pH~3 with 1M aqueous HCl solution. The acidic reaction mixture was filtered then the filter cake was collected and lyophilized to give the enriched *S*-enantiomer **P8a** (88.6. g, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 282.0. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 13.22 (br s, 1H), 4.66 – 4.34 (m, 2H), 3.86 – 3.60 (m, 1H), 3.12 – 2.82 (m, 2H), 1.41 (s, 9H), 1.17 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak IG-3 100 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2 / Mobile phase B: 50% MeOH with 0.2% of NH_3; backpressure: 1500 psi; flow rate: 2.8 mL/min; column temperature: 35 °C to provide **P8a**: major peak ((SFC-MS) *m/z* (M-*tert*-butyl group)$^+$ = 226.03 at retention time: 0.784 min, 96% ee)

Step 4. Preparation of (*S*)-5-(*tert*-butoxycarbonyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (+)-bis[(*R*)-1-phenylethyl]amine salt **(C21)**

The reaction was conducted in six batches in parallel then combined. To a mixture of **P8a** (0.180 kg, 0.640 mol) in EtOH (3.4 L) was added (+)-bis[(*R*)-1-phenylethyl]amine (CAS: 23294-41-9; 144 g, 0.640 mol) in one portion at room temperature to form the first batch. The

reaction mixture of the first batch was stirred at room temperature for 10 min then white precipitate formed. The suspension of the first batch was stirred at 80 °C for 1 h to form a clear solution then stirred at room temperature for 20 h. The white suspension of the first batch was filtered then the filter cake was washed with EtOH (3 x 300 mL).

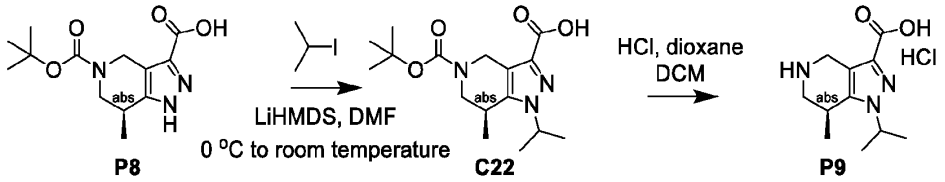
The filter cake from the first batch was collected then combined with the filter cakes from the additional five batches of the same reaction utilizing **P8a** (0.180 kg, 0.640 mol). The combined filter cake was dried in an oven at 50 °C for 18 h to provide **C21** (1.42 kg, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 282.1. ^{1}H NMR (400 MHz, CD_3OD) δ 7.46 – 7.36 (m, 6H), 7.29 – 7.23 (m, 4H), 4.76 – 4.53 (m, 2H), 3.95 – 3.86 (m, 2H), 3.83 – 3.70 (m, 1H), 3.25 – 3.18 (m, 1H), 2.99 – 2.89 (m, 1H), 1.52 (dd, 6H), 1.48 (s, 9H), 1.25 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak IG 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: MeOH with 0.05% of DEA; gradient: 20-40% of Mobile phase B over 1.5 min and hold 40% of Mobile phase B for 1.0 min then 20% of Mobile Phase B for 0.5 min; flow rate of 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide **C21:** peak 1 (retention time: 1.019 min, 100% ee).

Step 5. Preparation of (*S*)-5-(*tert*-butoxycarbonyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(P8)**

To a suspension of **C21** (48.2 g, 95.1 mmol) in H_2O (482 mL) was added 1M aqueous HCl solution (99 mL) to pH~1. The reaction mixture was stirred at room temperature for 1 h then filtered. The filter cake was collected then lyophilized to give **P8** (24.3 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 282.0. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 13.15 (br s, 1H), 4.63 – 4.47 (m, 1H), 4.44 – 4.33 (m, 1H), 3.84 – 3.61 (m, 1H), 3.19 – 3.00 (m, 1H), 2.94 – 2.83 (m, 1H), 1.41 (s, 9H), 1.17 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak IG-3 100 mm x 4.6 mm x 3 µm column; Mobile phase A: 50% of CO_2 / Mobile phase B: 50% of MeOH with 0.2% NH_3; backpressure: 1500 psi; flow rate: 2.8 mL/min; column temperature: 35 °C to provide **P8**: peak 1 ((SFC-MS) *m/z* (M-*tert*-butyl group)$^+$ = 226.00 at retention time: 0.757 min, 99% ee). $[\alpha]^{28}_D$=+11.351 (c= 1.5 (g/L in MeOH).

Preparation 9

(*S*)-1-Isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(P9)**



Step 1. Preparation of (*S*)-5-(*tert*-butoxycarbonyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C22)**

At 0 °C under nitrogen gas, to a solution of **P8** (12.4 g, 44.1 mmol) in DMF (220 mL) was added 1M LiHMDS (132 mL). The reaction mixture was warmed to room temperature and stirred for 2 h before cooling the reaction mixture again to 0 °C. To the cooled reaction mixture was added 2-iodopropane (11.2 g, 66.1 mmol) then the suspension was warmed to room temperature and stirred for 48 h. The reaction mixture was cooled to 0 °C and another portion of 2-iodopropane (1.12 g, 6.61 mmol) was added. The suspension was warmed to room temperature and stirred for 48 h. The reaction mixture was cooled to 0 °C then quenched with H_2O (500 mL). The aqueous phase was washed with EtOAc (2 x 200 mL) then the combined organic layer was discarded. The aqueous layer was acidified with 1M aqueous HCl to pH~3 then extracted with EtOAc (2 x 200 mL). The combined organic layer was washed with brine (2 x 300 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give **C22** (13.8 g, 96.8% yield) as a yellow solid. (LCMS) *m/z* $(M+H)^+$ = 324.0. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.60 (br s, 1H), 4.99 – 4.73 (m, 1H), 4.57 – 4.41 (m, 1H), 4.19 – 3.86 (m, 2H), 3.17 – 3.00 (m, 2H), 1.42 – 1.36 (m, 15H), 1.17 – 1.08 (m, 3H). The chiral purity was determined using SFC analytical method on (S,S) Whelk-01, 150 mm x 4.6 mm x 3.5 µm column; Mobile phase A: CO_2 / Mobile phase B: MeOH (0.2% isopropylamine); gradient: 10-50% of Mobile phase B in 6.00 min then held at 10% of Mobile phase B for 2.00 min; backpressure: 2000 psi; flow rate: 1.5 mL/min; column temperature: 35 °C to provide **C22**: peak 1 (retention time: 2.352 min, 100% ee). $[\alpha]^{34}_D$=-100.10 (c= 5.4 (g/L) in ACN).

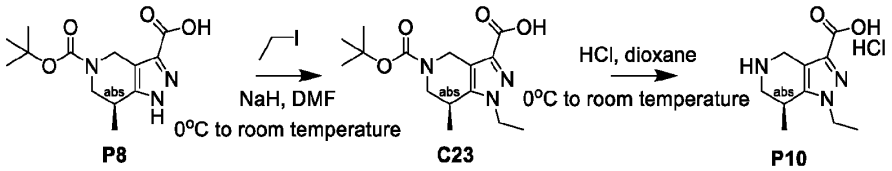
Step 2. Preparation of (*S*)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(P9)**

To a solution of **C22** (12.7 g, 39.3 mmol) in DCM (40 mL) was added 2M HCl in dioxane (500 mL). The reaction mixture was stirred at room temperature for 5 h then was concentrated *in vacuo* to provide **P9** (9.40 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 224.2. ^{1}H NMR (400 MHz, CD_3OD) δ 4.68 – 4.58 (m, 1H), 4.45 (d, 1H), 4.31 (d, 1H), 3.62 – 3.38 (m, 3H), 1.54 (d, 3H), 1.48 (d, 3H), 1.44 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralcel OX-3 100 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2 / Mobile phase B: MeOH containing

0.05% of DEA; gradient: 5-40% of Mobile Phase B in 3.0 min then held at 40% of Mobile phase B for 0.9 min then held at 5% of Mobile phase B for 0.1 min; backpressure: 100 bar; flow rate: 2.8 mL/min; column temperature: 40 °C to provide **P9**: peak 1 (retention time: 3.037 min, 100% ee). $[\alpha]^{33}_{D}$=-7.212 (c= 1.5 (g/L) in MeOH).

Preparation 10

(*S*)-1-Ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(P10)**



Step 1. Preparation of (*S*)-5-(*tert*-butoxycarbonyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C23)**

At 0 °C under nitrogen gas, to a solution of **P8** (10.0 g, 35.5 mmol) in DMF (190 mL) was added NaH (4.27 g, 107 mmol). The reaction mixture was stirred 0 °C for 30 min then a solution of iodoethane (6.65 g, 42.7 mmol) in DMF (10 mL) was added. The suspension was warmed to room temperature and stirred for 3 h then quenched with H_2O (150 mL). The aqueous phase was extracted with EtOAc (2 x 150 mL) then the combined organic layer was discarded. The aqueous phase was acidified with 1M aqueous HCl to pH~3 then extracted again with EtOAc (150 mL x3). The combined organic layer was washed with brine (2 x 100 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give a yellow solid. The solid was suspended in (1:10) EtOAc: PE (25 mL) and stirred at room temperature for 30 min. The suspension was filtered, and the filter cake was collected to provide **C23** (8.75 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 310.0. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.65 (br s, 1H), 4.85 (dd, 1H), 4.21 – 3.84 (m, 4H), 3.22 – 2.98 (m, 2H), 1.41 (br s, 9H), 1.35 (t, 3H), 1.16 – 1.08 (m, 3H). The chiral purity was determined using Chiral HPLC analytical method on Chiralcel OD-RH 150 mm x 4.6 mm x 5 µm column; Mobile phase A: H_2O (1.5 mL TFA) / Mobile phase B: ACN (1.5 mL TFA); gradient: 10-80% of Mobile phase B over 8 min then 10% of Mobile phase B in 1 min then a hold at 10% of Mobile phase B for 6 min, flow rate: 0.8 mL/min; column temperature: 30 °C to provide **C23**: peak 1 (retention time: 9.514 min, 100% ee). $[\alpha]^{34}_{D}$=-95.69 (c= 0.4 (g/L) in ACN).

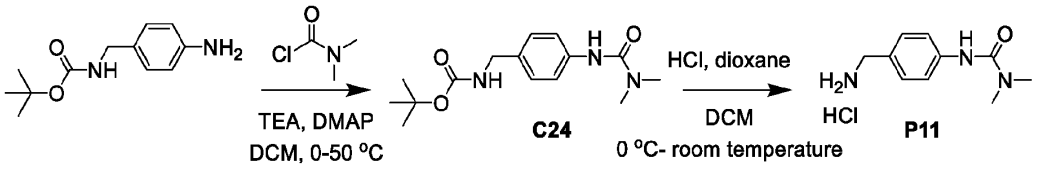
Step 2. Preparation of (*S*)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(P10)**

At 0 °C, to **C23** (8.00 g, 25.9 mmol) was added 2M HCl in dioxane (160 mL). The reaction mixture was stirred at room temperature for 4 h then was concentrated *in vacuo* to provide a yellow solid. The solid was dissolved in 2M HCl in dioxane (40 mL) and stirred at

room temperature for 2 h then was concentrated *in vacuo* to provide **P10** (7.10 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 210.2. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.97 (br s, 1H), 10.05 (s, 1H), 9.49 (s, 1H), 4.23 – 4.03 (m, 4H), 3.41 – 3.30 (m, 2H), 3.26 – 3.18 (m, 1H), 1.39 – 1.32 (m, 6H). The chiral purity was determined using SFC analytical method on Chiralcel OX-3 100 mm x 4.6 mm, 3 µm column; Mobile phase A: CO_2/ Mobile phase B: MeOH with 0.05% of DEA; Isocratic: 40% of Mobile phase B; backpressure: 100 bar; flow rate: 2.8 mL/min; column temperature: 40 °C to provide **P10**: peak 1 (retention time: 1.631 min, 100% ee). $[\alpha]^{33}_D$=-1.584 (c= 1.5 (g/L) in MeOH).

Preparation 11

3-(4-(Aminomethyl)phenyl)-1,1-dimethylurea hydrochloride **(P11)**



Step 1. Preparation of *tert*-butyl (4-(3,3-dimethylureido)benzyl)carbamate **(C24)**

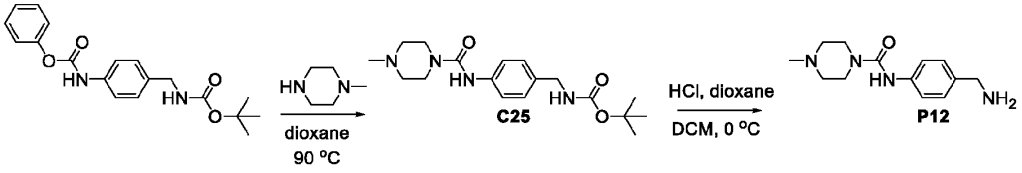
At 0 °C under nitrogen gas, to a solution of *tert*-butyl (4-aminobenzyl)carbamate (CAS: 94838-55-8; 15.0 g, 67.5 mmol) in DCM (150 mL), TEA (20.5 g, 202 mmol) and DMAP (0.824 g, 6.75 mmol) was added dimethylcarbamic chloride (14.5 g, 135 mmol) dropwise. The reaction mixture was stirred at 50 °C for 16 h then was diluted with MeOH (150 mL) and concentrated *in vacuo* to give a residue. The residue was suspended in H_2O (120 mL) then rapidly stirred at room temperature for 1 h. The suspension was filtered then the filter cake was collected and triturated with MeOH: EtOAc: MTBE (5 mL: 25 mL: 250 mL) at room temperature for 1 h. The suspension was filtered, and the filter cake was collected then concentrated *in vacuo* to provide **C24** (14.6 g, 73.8% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 294.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.21 (s, 1H), 7.37 (d, 2H), 7.30 (t, 1H), 7.08 (d, 2H), 4.03 (d, 2H), 2.91 (s, 6H), 1.39 (s, 9H)

Step 2. Preparation of 3-(4-(aminomethyl)phenyl)-1,1-dimethylurea hydrochloride **(P11)**

At 0 °C, to a stirred suspension of **C24** (23 g, 71 mmol) in DCM (130 mL) was added 2M HCl in dioxane (270 mL) dropwise. The reaction mixture was stirred at room temperature for 3 h then was concentrated *in vacuo* to provide **P11** (15 g, 83.4%) as a yellow solid. The solid was used directly in the next step without additional purification. (LC/MS) m/z $(2M+H)^+$ = 387.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.40 (s, 1H), 8.25 (br s, 2H), 7.53 - 7.47 (m, 2H), 7.35 - 7.29 (m, 2H), 3.91 (q, 2H), 2.92 (s, 6H).

Preparation 12

N-(4-(Aminomethyl)phenyl)-4-methylpiperazine-1-carboxamide hydrochloride **(P12)**



Step 1. Preparation of *tert*-butyl (4-(4-methylpiperazine-1-carboxamido)benzyl)carbamate **(C25)**

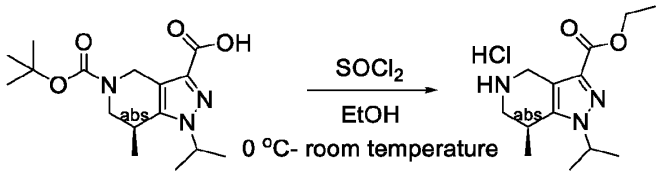
To a solution of phenyl (4-(((*tert*-butoxycarbonyl)amino)methyl)phenyl)carbamate (CAS: 1632297-04-2; 8.0 g, 23 mmol) in dioxane (120 mL) was added 1-methylpiperazine (CAS: 109-01-3; 2.8 g, 28 mmol). The reaction mixture was stirred at 90 °C overnight. The suspension was diluted with EtOAc (100 mL) and washed with 1M NaOH (2 x 50 mL) then brine (50 mL). The organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. The residue was triturated with PE (2 x 50 mL) over 20 min then the suspension was filtered. The filter cake was collected to provide **C25** (7.7 g, crude) as a brown solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 349.2. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.44 (s, 1H), 7.35 (d, 2H), 7.28 (t, 1H), 7.07 (d, 2H), 4.05 – 3.95 (m, 2H), 3.40 (t, 4H), 2.29 (t, 4H), 2.18 (s, 3H), 1.40 – 1.32 (m, 9H).

Step 2. Preparation of *N*-(4-(aminomethyl)phenyl)-4-methylpiperazine-1-carboxamide hydrochloride **(P12)**

To a stirred solution of **C25** (7.7 g, 22 mmol) in DCM (20 mL) was added HCl in dioxane (0.050 g, 1.4 mmol). The reaction mixture was stirred at 0 °C for 4 h then concentrated *in vacuo* and lyophilized to provide **P12** (6.9 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 249.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 11.27 (br s, 1H), 9.08 (s, 1H), 8.36 (br s, 3H), 7.53 – 7.47 (m, 2H), 7.34 – 7.29 (m, 2H), 4.25 (d, 2H), 3.87 (q, 2H), 3.31 – 3.18 (m, 2H), 3.04 – 2.89 (m, 2H), 2.72 (s, 3H).

Preparation 13

Ethyl (*S*)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P13)**

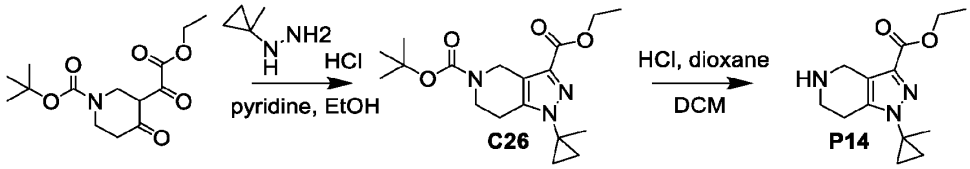


Step 1. Preparation of ethyl (*S*)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P13)**

To a stirred solution of **C22** (0.500 g, 1.55 mmol) in EtOH (3 mL) was added $SOCl_2$ (1.29 g, 10.8 mmol) dropwise at 0 °C. The reaction mixture was stirred at room temperature for 66 h then concentrated *in vacuo* to provide **P13** (0.426 g, 95.7% yield) as a light-yellow solid. (LC/MS) m/z $(M+H)^+$ = 252.2.

Preparation 14

Ethyl 1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P14)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-(1-methylcyclopropyl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C26)**

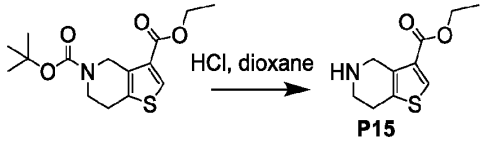
The same procedure was followed from **Preparation 2, step 1** with *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 0.577 g, 1.93 mmol) and (1-methylcyclopropyl)hydrazine hydrochloride (CAS: 2737246-42-1, 0.166 g, 1.93 mmol). The residue was purified by column chromatography (silica gel, 0-30% EtOAc: PE) to provide **C26** (0.233 g, 34.6% yield) as a light-brown oil. (LC/MS) m/z $(M+H)^+$ = 350.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.58 (s, 2H), 4.38 (q, 2H), 3.74 – 3.66 (m, 2H), 2.83 – 2.74 (m, 2H), 1.52 (s, 3H), 1.48 (s, 9H), 1.37 (t, 3H), 1.28 – 1.23 (m, 2H), 0.97 – 0.91 (m, 2H).

Step 2. Preparation of ethyl 1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P14)**

The same procedure was followed from **Preparation 5, step 2** with **C26** (0.233 g, 0.667 mmol) to provide **P14** (0.191 g, crude) as a light-yellow solid, which was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 250.1. ^{1}H NMR (400 MHz, CD_3OD) δ 4.39 – 4.33 (m, 2H), 3.66 (s, 2H), 3.56 (t, 2H), 3.19 (t, 2H), 1.55 (s, 3H), 1.38 (t, 3H), 1.31 – 1.26 (m, 2H), 1.09 – 1.04 (m, 2H).

Preparation 15

Ethyl 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine-3-carboxylate hydrochloride **(P15)**



Step 1. Preparation of ethyl 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine-3-carboxylate hydrochloride **(P15)**

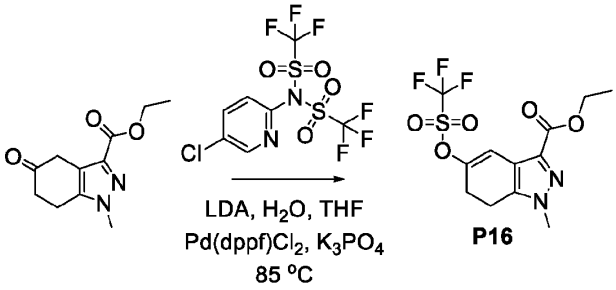
The same reaction was conducted in two batches then combined. To 5-(*tert*-butyl) 3-ethyl 6,7-dihydrothieno[3,2-*c*]pyridine-3,5(4*H*)-dicarboxylate (CAS: 1363381-39-8; 50.0 mg,

0.161 mmol) was added HCl in dioxane (0.234 g, 6.42 mmol) to form the first batch. The solution of the first batch was stirred at room temperature for 2 h then concentrated *in vacuo* to provide a white solid.

A second batch of the same reaction was conducted with 5-(*tert*-butyl) 3-ethyl 6,7-dihydrothieno[3,2-*c*]pyridine-3,5(4*H*)-dicarboxylate (CAS: 1363381-39-8; 0.450 g, 1.45 mmol). The solids from the two batches were combined to provide **P15** (0.339 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 212.0.

Preparation 16

Ethyl 1-methyl-5-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-1*H*-indazole-3-carboxylate **(P16)**

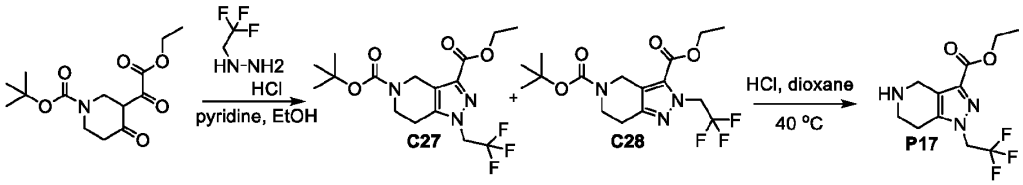


Step 1. Preparation of ethyl 1-methyl-5-(((trifluoromethyl)sulfonyl)oxy)-6,7-dihydro-1*H*-indazole-3-carboxylate **(P16)**

To a suspension of ethyl 1-methyl-5-oxo-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxylate (CAS: 2090404-84-3; 0.500 g, 1.41 mmol) and *N*-(5-chloropyridin-2-yl)-1,1,1-trifluoro-*N*-((trifluoromethyl)sulfonyl)methanesulfonamide (CAS: 145100-51-2; 0.409 g, 2.12 mmol) in H_2O (1 mL) and THF (10 mL) was added $Pd(dppf)Cl_2$ (0.103 g, 0.141 mmol) and K_3PO_4 (0.899 g, 4.23 mmol). The reaction mixture was degassed with nitrogen gas and stirred at 85 °C for 16 h then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-38% THF: PE) to provide **P16** (0.470 g, 94.2% yield) as a pink solid. (LC/MS) m/z $(M+H)^+$ = 355.0

Preparation 17

Ethyl 1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P17)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-(2,2,2-trifluoroethyl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C27)** and 2-((3-(ethoxycarbonyl)-2-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C28)**

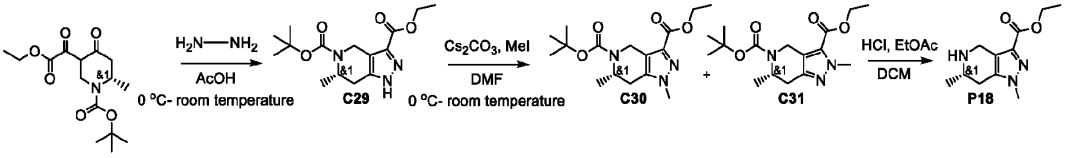
To a suspension of (2,2,2-trifluoroethyl)hydrazine hydrochloride (CAS: 1081515-82-3; 0.226 g, 1.50 mmol) in EtOH (5 mL) and pyridine (0.476 g, 6.01 mmol) was added *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 0.450 g, 1.50 mol). The reaction mixture was stirred at room temperature for 17 h then was checked by LCMS which showed the major isomer of **C27** [LC/MS) m/z (M-*tert*-butyl group)$^+$ = 321.9 at 0.87 min retention time] and the minor isomer of **C28** [(LC/MS) m/z (M+H)$^+$ = 378.2 at 0.94 min retention time]. The suspension was concentrated *in vacuo* then dissolved in DCM and purified by column chromatography (silica gel, 0-40% EtOAc: heptane) to provide the major isomer of **C27** (eluted at 30-40% EtOAc: heptane) (0.344 g, 60.7% yield) as a yellow oil. (LC/MS) m/z (M-*tert*-butyl group)$^+$ = 322.2. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.69 (q, 2H), 4.62 (br s, 2H), 4.41 (q, 2H), 3.77 – 3.70 (m, 2H), 2.74 – 2.70 (m, 2H), 1.56-1.43 (m, 9H), 1.40 (t, 3H)

Step 2. Preparation of ethyl 1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P17)**

To a solution of **C27** (0.344 g, 0.912 mmol) in DCM (5.0 mL) was added 4M HCl in dioxane (1.4 mL). The reaction solution was stirred at 40 °C for 24 h then concentrated *in vacuo* to provide **P17** (0.328 g, crude) as a white solid. (LC/MS) m/z (M+H)$^+$ = 278.2. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 9.20 (br s, 1H), 5.31 (q, 2H), 4.32 – 4.22 (m, 4H), 3.39 (t, 2H), 2.99 (t, 2H), 1.29 – 1.26 (m, 3H).

Preparation 18

rac-Ethyl (*R*)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P18)**



Step 1. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-6-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C29)**

At 0 °C, to a suspension of *rac-tert*-butyl *(2R)*-5-(2-ethoxy-2-oxoacetyl)-2-methyl-4-oxopiperidine-1-carboxylate (CAS: 2386748-67-8; 24 g, 77 mmol) in AcOH (120 mL) was added hydrazine monohydrate (CAS: 7803-57-8; 14 g, 0.18 mol) dropwise via addition funnel. The reaction was stirred at room temperature for 1 h then concentrated *in vacuo*. The residue was diluted in EtOAc (200 mL) then washed with aqueous $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide **C29** (23 g, crude) as an orange

viscous liquid. The liquid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 310.2. ^1H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 5.06 (d, 1H), 4.85 (s, 1H), 4.44 – 4.28 (m, 2H), 4.15 – 4.10 (m, 1H), 2.96 (dd, 1H), 2.67 – 2.58 (m, 1H), 1.48 – 1.46 (m, 9H), 1.44 – 1.32 (m, 3H), 1.10 (d, 3H).

Step 2. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1,6-dimethyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C30)** and *rac*-(*R*)-2-((3-(ethoxycarbonyl)-2,6-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C31)**

At 0 °C, to a solution **C29** (23 g, 74 mmol) in DMF (200 mL) was added Cs_2CO_3 (27 g, 82 mmol) and MeI (14 mL) dropwise. The reaction mixture was stirred at room temperature for 20 h then concentrated *in vacuo*. The residue was dissolved in MTBE (200 mL) then wash with H_2O (200 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to form an orange oil. The residue was purified by column chromatography (silica gel, 0-100% isopropyl acetate: heptane) to provide **C30** (3.0 g, 25% yield) and **C31** (1.6 g, 14% yield).

C30: (LC/MS) m/z $(M+H)^+$ = 324.2. ^1H NMR (400 MHz, $CDCl_3$) δ 5.12 – 4.92 (m, 1H), 4.87 – 4.72 (m, 1H), 4.41 – 4.23 (m, 2H), 4.11 (s, 3H), 4.10 – 4.02 (m, 1H), 2.90 (dd, 1H), 2.59 – 2.48 (m, 1H), 1.48 – 1.44 (m, 9H), 1.39 – 1.34 (m, 3H), 1.09 (d, 3H).

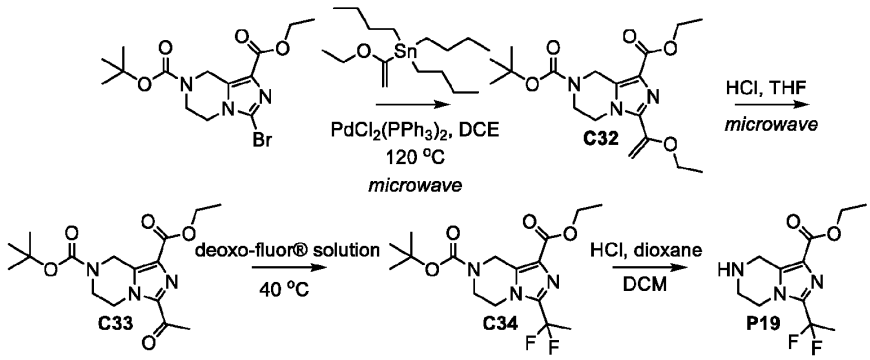
C31: (LC/MS) m/z $(M+H)^+$ = 324.2. ^1H NMR (400 MHz, $CDCl_3$) δ 5.08 – 4.85 (m, 2H), 4.44 – 4.30 (m, 2H), 4.08 (d, 1H), 3.80 (s, 3H), 2.94 – 2.84 (m, 1H), 2.44 – 2.38 (m, 1H), 1.46 (s, 9H), 1.37 (t, 3H), 1.20 (d, 3H).

Step 3. Preparation of *rac*-ethyl (*R*)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P18)**

To a solution of **C30** (0.460 g, 1.42 mmol) in DCM (5 mL) was added 1M HCl in EtOAc (5 mL). The reaction solution was stirred at room temperature for 6 h then concentrated *in vacuo* to provide **P18** (0.325 g, crude) as a white foam, which was used directly in the next step without further purification.

Preparation 19

Ethyl 3-(1,1-difluoroethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(P19)**



Step 1. Preparation of 7-(*tert*-butyl) 1-ethyl 3-(1-ethoxyvinyl)-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C32)**

To a solution of 7-(*tert*-butyl) 1-ethyl 3-bromo-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (CAS: 2108354-93-2; 1.50 g, 4.01 mmol) in DCE (30 mL) was added tributyl(1-ethoxyvinyl)tin (CAS: 97674-02-7; 4.45 g, 12.3 mmol) and $PdCl_2(PPh_3)_2$ (0.422 g, 0.601 mmol). The reaction mixture was stirred in a microwave at 120 °C for 30 min then was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel; 0-27% THF: PE) to provide **C32** (0.960 g, 65.5% yield) as an oil. (LC/MS) m/z $(M+H)^+$ = 366.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.06 (d, 1H), 4.90 (s, 2H), 4.42 – 4.33 (m, 2H), 4.18 (t, 2H), 3.90 (q, 2H), 3.79 – 3.71 (m, 3H), 1.50 (br s, 9H), 1.44 – 1.33 (m, 6H).

Step 2. Preparation of 7-(*tert*-butyl) 1-ethyl 3-acetyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C33)**

To a solution of **C32** (0.660 g, 1.81 mmol) in THF (12 mL) was added 2M HCl (0.132 g, 3.61 mmol). The reaction mixture was stirred in the microwave for 16 h then the clear yellow solution was concentrated *in vacuo*. The residue was poured into saturated $NaHCO_3$ then extracted with EtOAc (3 x 20 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The brown residue was purified by column chromatography (silica gel, 0-20% EtOAc: PE) to provide **C33** (0.440 g, 81.1% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 338.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.95 (s, 2H), 4.47 (t, 2H), 4.41 (q, 2H), 3.79 (t, 2H), 2.70 (s, 3H), 1.50 (s, 9H), 1.41 (t, 3H).

Step 3. Preparation of 7-(*tert*-butyl) 1-ethyl 3-(1,1-difluoroethyl)-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C34)**

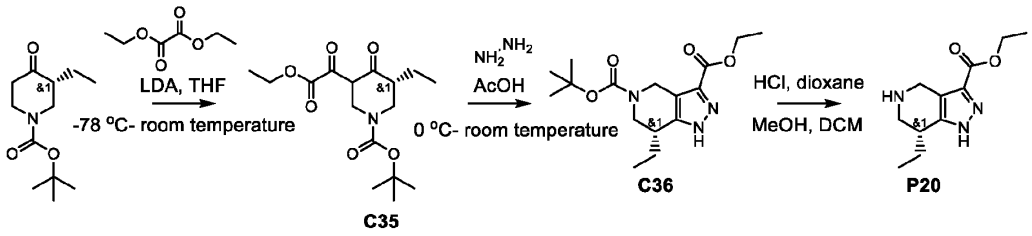
A solution of **C33** (0.435 g, 1.29 mmol) in deoxo-fluor™ solution (CAS: 202289-38-1; 10 mL) was stirred at 40 °C for 72 h. The reaction mixture was cooled to room temperature then extracted with DCM (2 x 20 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-20% EtOAc: PE) to provide **C34** (0.310 g, 66.9% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 360.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (s, 2H), 4.38 (q, 2H), 4.25 (t, 2H), 3.83 (t, 2H), 2.19 (t, 3H), 1.50 (s, 9H), 1.39 (t, 3H).

Step 4. Preparation of ethyl 3-(1,1-difluoroethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(P19)**

To a solution of **C34** (0.310 g, 0.863 mmol) in DCM (3 mL) was added 2M HCl in dioxane (6 mL). The reaction mixture was stirred at room temperature for 16 h then concentrated *in vacuo* and dried further by high *vacuo* to provide **P19** (0.255 g, crude) as a gum. The gum was used directly in the next step without further purification.

Preparation 20

rac-Ethyl (*R*)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P20)**



Step 1. Preparation of *rac-tert*-butyl *(5R)*-3-(2-ethoxy-2-oxoacetyl)-5-ethyl-4-oxopiperidine-1-carboxylate **(C35)**

At -78 °C under nitrogen gas in a 250 mL three-neck round bottom flask, LDA (4.24 g, 39.6 mmol) was added to THF (25 mL). To the solution at -78 °C, *tert*-butyl 3-ethyl-4-oxopiperidine-1-carboxylate (CAS: 117565-57-8; 9.00 g, 39.6 mmol) in THF (60 mL) was added dropwise then stirred at -78°C for 1 h. After the stir, a solution of diethyl oxalate (5.79 g, 39.6 mmol) in THF (20 mL) was added dropwise at -78 °C then stirred at -78 °C for 1 h. The reaction mixture warmed to room temperature then stirred for 16 h. The suspension was cooled to 0 °C then quenched with 1M aqueous $KHSO_4$ (150 mL) and filtered. The filtrate was extracted with EtOAc (2 x 200 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide **C35** (13.0 g, crude) as a yellow gum. The gum was used directly in the next step without further purification. (LC/MS) m/z (M-*tert*-butyl group)$^+$ = 272.0. ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.42 (br s, 1H), 4.53 – 4.16 (m, 4H), 3.68 – 3.32 (m, 2H), 2.44 – 2.32 (m, 1H), 1.84 – 1.67 (m, 1H), 1.53 – 1.42 (m, 2H), 1.41 – 1.39 (m, 9H), 1.31 (t, 3H), 0.97 (t, 3H).

Step 2. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-7-ethyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C36)**

The same procedure was followed from **Preparation 18, step 1** with **C35** (6.00 g, 18.3 mmol) to provide **C36** (8.89 g, crude) as a yellow gum, which was used directly in the next step without further purification**.** (LC/MS) m/z (M+H)$^+$ = 324.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (br s, 1H), 4.93 – 4.44 (m, 2H), 4.37 (q, 2H), 3.83 – 3.68 (m, 1H), 3.57 – 3.41 (m, 1H), 2.88 – 2.71 (m, 1H), 1.84 – 1.70 (m, 1H), 1.62 – 1.51 (m, 2H), 1.50 – 1.48 (m, 9H), 1.38 (t, 3H), 1.05 (t, 3H).

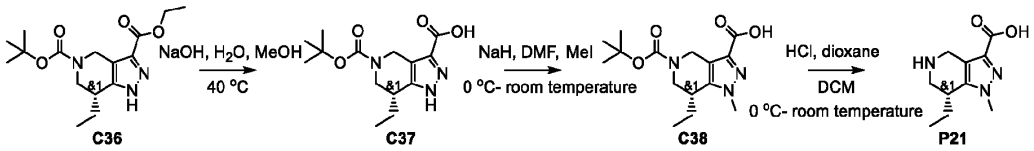
Step 3. Preparation of *rac*-ethyl (*R*)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P20)**

To a suspension of **C36** (0.400 g, 1.24 mmol) in DCM (6 mL) and MeOH (2 mL) was added 2M HCl in dioxane (3 mL). The reaction mixture was stirred at room temperature for 2 h then an additional portion of 2M HCl in dioxane (3 mL) was added. The suspension was stirred

for 16 h at room temperature then concentrated *in vacuo* to provide **P20** (0.276 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.68 (br s, 2H), 4.37 – 4.11 (m, 4H), 3.52 – 3.44 (m, 1H), 3.14 – 3.06 (m, 1H), 3.05 – 2.94 (m, 1H), 1.99 – 1.85 (m, 1H), 1.67 – 1.53 (m, 1H), 1.29 (t, 3H), 0.94 (t, 3H).

Preparation 21

rac-(*R*)-7-Ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(P21)**



Step 1. Preparation of *rac*-(*R*)-5-(*tert*-butoxycarbonyl)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C37)**

To a suspension of **C36** (2.00 g, 6.18 mmol) in MeOH (6.6 mL) and H_2O (6.6 mL) was added NaOH (0.495 g, 12.4 mmol). The reaction mixture was stirred at 40 °C for 2 h then was diluted with H_2O (20 mL). The diluted reaction mixture was cooled to 0 °C then acidified with 1M aqueous HCl to pH~3 and filtered. The filter cake was collected to provide **C37** (1.60 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 296.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 13.15 (br s, 1H), 4.73 – 4.24 (m, 2H), 3.74 - 3.41 (m, 2H), 2.78 – 2.67 (m, 1H), 1.70 (br s, 1H), 1.49 – 1.40 (m, 10H), 1.02 (t, 3H).

Step 2. Preparation of *rac*-(*R*)-5-(*tert*-butoxycarbonyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C38)**

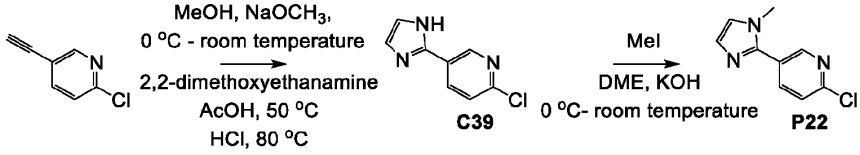
The same procedure was followed from **Preparation 3, step 2** with **C37** (1.00 g, 3.39 mmol) and MeI (0.577 g, 4.06 mmol) to provide **C38** (0.850 g, crude) as a white solid, which was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 310.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.65 (br s, 1H), 5.01 – 4.75 (m, 1H), 4.34 – 3.88 (m, 2H), 3.79 (s, 3H), 3.07 – 2.67 (m, 2H), 1.63 – 1.50 (m, 1H), 1.43 (s, 9H), 1.36 – 1.23 (m, 1H), 1.08 – 0.95 (m, 3H).

Step 3. Preparation of *rac*-(*R*)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(P21)**

At 0 °C, to a solution of **C38** (0.300 g, 0.970 mmol) in DCM (1 mL) was added HCl in dioxane (2 mL). The reaction mixture was warmed to room temperature and stirred for 16 h then concentrated *in vacuo* to provide **P21** (0.236 g, crude) as a yellow solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.97 (br s, 1H), 9.70 (br s, 1H), 9.13 (br s, 1H), 4.27 – 4.03 (m, 2H), 3.86 (s, 3H), 3.32 – 3.08 (m, 3H), 1.81 – 1.66 (m, 2H), 0.97 (t, 3H).

Preparation 22

2-Chloro-5-(1-methyl-1*H*-imidazol-2-yl)pyridine **(P22)**



Step 1. Preparation of 2-chloro-5-(1*H*-imidazol-2-yl)pyridine **(C39)**

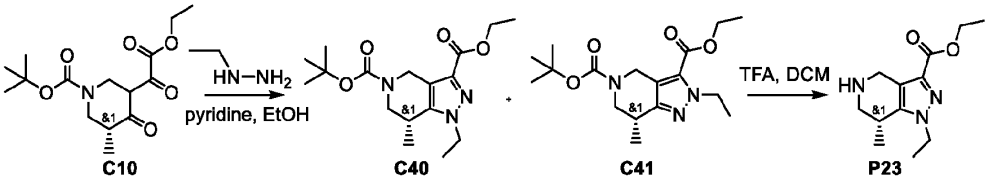
At 0 °C, to a solution of 2-chloro-5-ethynylpyridine (CAS: 263012-63-1, 94.0 g, 680. mmol) in MeOH (1.5 L) was added $NaOCH_3$ (5.50 g, 102 mmol). The reaction was stirred at room temperature for 1 h before 2,2-dimethoxyethanamine (71.3 g, 678 mmol) and AcOH (81.5 g, 1.36 mol) were added. The reaction was stirred at 50 °C for 1 h then cooled to room temperature before 6M HCl (74.2 g, 2.04 mol) was added. The reaction was stirred at 80 °C for 5 h then concentrated *in vacuo.* The residue was extracted with EtOAc (2 x 500 mL). The aqueous layer was adjusted to pH=10 with saturated aqueous Na_2CO_3 solution which caused white solid precipitate to form. The suspension was filtered then the filter cake was washed with H_2O (3 x 100 mL). The filter cake was collected then lyophilized to provide **C39** (88.0 g, 72.2% yield) as a white solid. The solid was used directly in the next step without additional purification. (LC/MS) m/z $(M+H)^+$ = 180.0. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 12.77 (br s, 1H), 8.94 (d, 1H), 8.31 (dd, 1H), 7.62 (d, 1H), 7.22 (s, 2H).

Step 2. Preparation of 2-chloro-5-(1-methyl-1*H*-imidazol-2-yl)pyridine **(P22)**

To a solution of **C39** (44.0 g, 204 mmol) in DME (440 mL) was added KOH (24.0 g, 428 mmol) at room temperature then stirred for 1 h and 40 min. The reaction mixture was cooled to 0 °C before MeI (57.8 g, 407 mmol) was added then stirred at 0 °C for 1 h. The white suspension was filtrated then concentrated *in vacuo*. The residue was washed with H_2O (300 mL) and stirred for 30 min. The reaction mixture was filtered, and the filter cake was concentrated *in vacuo* to provide **P22** (34.8 g, 88.8% yield) as a white solid. The solid was used directly in the next step without additional purification. (LC/MS) m/z $(M+H)^+$ = 194.0. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.79-8.76 (m, 1H), 8.20 (dd, 1H), 7.68-7.64 (m, 1H), 7.37 (d, 1H), 7.08 (d, 1H), 3.83 (s, 3H).

Preparation 23

rac-Ethyl (*R*)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate trifluoroacetate **(P23)**



Step 1. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1-ethyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C40)** and *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-2-ethyl-7-methyl-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C41)**

A suspension of **C10** (1.00 g, 3.19 mmol) and ethylhydrazine dihydrochloride (CAS: 49540-34-3; 0.425 g, 3.19 mmol) in EtOH (20 mL) and pyridine (1.11 g, 14.0 mmol) was stirred at room temperature for 16 h. The reaction mixture was concentrated *in vacuo* then purified by column chromatography (silica gel, 0-40% EtOAc: PE) to provide **C41** (0.290 g, 26.9% yield) as a light-yellow solid and **C40** (0.700 g, 65.0% yield) as a light-yellow gum.

C40: (LC/MS) m/z $(M+H)^+$ = 338.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 – 4.88 (m, 1H), 4.44 – 4.32 (m, 2H), 4.29 – 3.97 (m, 4H), 3.16 (d, 1H), 3.00 – 2.88 (m, 1H), 1.52 – 1.44 (m, 12H), 1.38 (t, 3H), 1.25 (d, 3H).

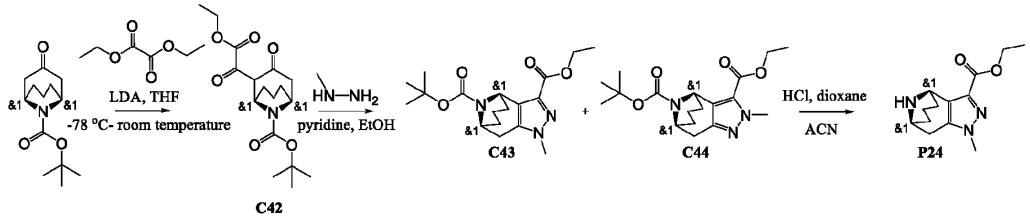
C41: (LC/MS) m/z $(M+H)^+$ = 338.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 – 4.46 (m, 4H), 4.33 (q, 2H), 3.96 – 3.64 (m, 1H), 3.36 – 3.08 (m, 1H), 3.00 – 2.91 (m, 1H), 1.50 – 1.44 (m, 9H), 1.39 (q, 6H), 1.26 (d, 3H).

Step 2. Preparation of *rac*-ethyl (*R*)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate trifluoroacetate **(P23)**

To a solution of **C40** (0.250 g, 0.741 mmol) in DCM (4 mL) was added TFA (2 mL). The reaction mixture was stirred at room temperature for 2 h then concentrated *in vacuo* to provide **P23** (0.260 g, crude) as a colorless gum, which was used directly in the next step without further purification.

Preparation 24

rac-Ethyl (*4R,8S*)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxylate **(P24)**



Step 1. Preparation of *rac-tert*-butyl (*1R,5S*)-2-(2-ethoxy-2-oxoacetyl)-3-oxo-9-azabicyclo[3.3.1]nonane-9-carboxylate **(C42)**

At -78 °C, LDA (1.07 g, 10.0 mmol) was added to THF (50 mL). To the solution at -78 °C, *tert*-butyl (*1R,5S*)-3-oxo-9-azabicyclo[3.3.1]nonane-9-carboxylate (CAS: 512822-27-4; 2.00 g, 8.36 mmol) in THF (50 mL) was added dropwise and then stirred at -78 °C for 1 h. After the stir, a solution of diethyl oxalate (1.28 g, 8.78 mmol) in THF (20 mL) was added dropwise at -78 °C and then stirred at -78 °C for 30 min. The reaction mixture was warmed to room temperature, stirred for 1 h, and then concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, 2-16% EtOAc: PE) to provide **C42** (0.750 g, 26.4% yield) as a light yellow oil. (LC/MS) m/z $(M+H)^+$ = 340.1 ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49 (d, 1H), 4.77 – 4.48 (m, 2H), 4.36 (q, 2H), 2.98 – 2.81 (m, 1H), 2.44 – 2.31 (m, 1H), 1.86 – 1.72 (m, 3H), 1.69 – 1.58 (m, 3H), 1.50 – 1.42 (m, 9H), 1.39 (t, 3H).

Step 2. Preparation of *rac*-10-(*tert*-butyl) 3-ethyl (*4R,8S*)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3,10-dicarboxylate **(C43)** and *rac*-10-(*tert*-butyl) 3-ethyl (*4R,8S*)-2-methyl-4,5,6,7,8,9-hexahydro-2*H*-4,8-epiminocycloocta[*c*]pyrazole-3,10-dicarboxylate **(C44)**

To a solution of **C42** (0.650 g, 2.17 mmol) in EtOH (20 mL) was added methylhydrazine dihydrochloride (CAS: 55330-60-4; 0.179 g, 2.17 mmol) and pyridine (0.859 g, 10.9 mmol). The reaction mixture was stirred at room temperature for 16 h and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 12-100% EtOAc: PE) to provide **C43** (0.390 g, 51.4% yield) as an oil and **C44** (0.150 g, 19.8% yield).

C43: (LC/MS) m/z $(M+H)^+$ = 350.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 – 5.53 (m, 1H), 4.79 – 4.57 (m, 1H), 4.46 – 4.28 (m, 2H), 3.80 (s, 3H), 3.11 – 2.95 (m, 1H), 2.43 (d, 1H), 1.89 – 1.69 (m, 4H), 1.63 – 1.55 (m, 1H), 1.50 – 1.41 (m, 10H), 1.40 – 1.34 (m, 3H).

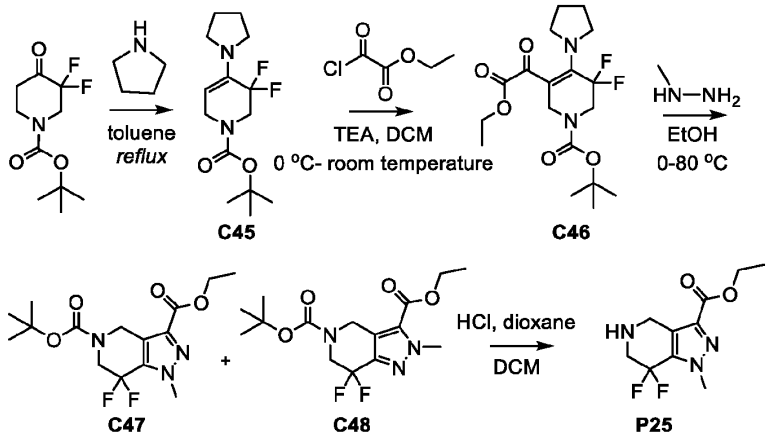
C44: (LC/MS) m/z (M+H)+ = 350.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 – 5.48 (m, 1H), 4.78 – 4.53 (m, 1H), 4.45 – 4.19 (m, 2H), 4.15 – 4.07 (m, 3H), 3.19 – 3.00 (m, 1H), 2.63 – 2.52 (m, 1H), 1.90 – 1.58 (m, 5H), 1.44 (s, 10H), 1.38 (t, 3H).

Step 3. Preparation of *rac*-ethyl (*4R,8S*)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxylate **(P24)**

To a solution of **C43** (0.222 g, 0.636 mmol) in ACN (6 mL) was added HCl in dioxane (0.116 g, 3.18 mmol). The reaction mixture was stirred at room temperature for 16 h then concentrated *in vacuo* to provide **P24** (0.150 g, crude) as a white solid. The solid was used directly in the next step without further purification.

Preparation P25

Ethyl 7,7-difluoro-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P25)**



Step 1. Preparation of *tert*-butyl 3,3-difluoro-4-(pyrrolidin-1-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate **(C45)**

To a solution of *tert*-butyl 3,3-difluoro-4-oxopiperidine-1-carboxylate (CAS:1215071-17-2; 3.00 g, 11.8 mmol) in toluene (40 mL) was added pyrrolidine (0.927 g, 13.0 mmol). The reaction mixture was heated for 20 h using a Deans and Stark trap to remove the H_2O liberated during the reaction, then concentrated *in vacuo* to provide **C45** (3.42 g, crude) as a brown solid. The solid was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 – 4.46 (m, 1H), 4.14 – 4.05 (m, 2H), 3.90 (t, 2H), 3.20 – 3.13 (m, 4H), 1.97 – 1.88 (m, 4H), 1.53 (s, 9H).

Step 2. Preparation of *tert*-butyl 5-(2-ethoxy-2-oxoacetyl)-3,3-difluoro-4-(pyrrolidin-1-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate **(C46)**

A solution of **C45** (3.42 g, 11.9 mmol) in DCM (50 mL) was degassed with nitrogen gas for 10 min. The reaction mixture was cooled to 0 °C before ethyl oxalyl chloride (1.94 g, 14.2 mmol) was added dropwise over 15 min. The temperature was maintained between (0-5) °C throughout the addition. Following the addition, TEA (1.80 g, 17.8 mmol) was added dropwise over 5 min. The reaction mixture was warmed to room temperature and stirred for 5 h, then diluted with H_2O (300 mL). The diluted reaction mixture was extracted with DCM (3 x 100 mL). The combined organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-25% EtOAc: PE) to provide **C46** (2.98 g, 64.7% yield) as a yellow solid. (LC/MS) m/z $(M+H)^+$ = 389.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (s, 2H), 4.30 (q, 2H), 3.89 (t, 2H), 3.49 – 3.41 (m, 4H), 2.00 – 1.94 (m, 4H), 1.48 (s, 9H), 1.35 (t, 3H).

Step 3. Preparation of 5-(*tert*-butyl) 3-ethyl 7,7-difluoro-1-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C47)** and 2-((3-(ethoxycarbonyl)-7,7-difluoro-2-methyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C48)**

The reaction was conducted in three batches and then combined for further purification. At 0 °C, to a solution of **C46** (1.09 g, 2.81 mmol) in EtOH (10 mL) was added methylhydrazine dihydrochloride (CAS: 55330-60-4; 0.402 g, 3.38 mmol) dropwise over 5 min then the reaction was sealed and stirred at 80 °C for 2 h to form the first batch.

The second batch of the same reaction was conducted with **C46** (0.500 g, 1.29 mmol), and the third batch was conducted with **C46** (0.100 g, 0.257 mmol). The batches were combined and then diluted with H_2O (60 mL). The diluted reaction mixture was extracted with EtOAc (3 x 50 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-15% EtOAc: PE) to provide **C48** (0.756 g, 50.4% yield) as brown oil and an impure **C47** as a residue. The residue, **C47**, was purified by reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O (0.05% NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 32 to 72% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate= 60 mL/min) and lyophilized to provide **C47** (0.416 g, 27.7% yield) as a colorless oil.

C47: (LC/MS) m/z (M-*tert*-butyl group)$^+$ = 290.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.69 (br s, 2H), 4.41 (q, 2H), 4.09 – 3.96 (m, 5H), 1.49 (s, 9H), 1.40 (t, *3*H).

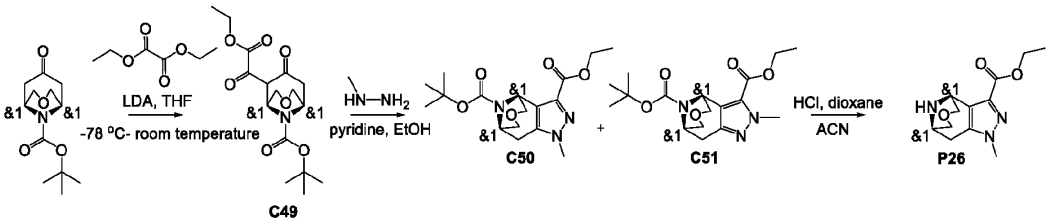
C48: (LC/MS) m/z (M-*tert*-butyl group)$^+$ = 290.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.73 – 4.63 (m, 2H), 4.37 (q, 2H), 4.23 (s, 3H), 4.06 – 3.95 (m, 2H), 1.49 (s, 9H), 1.40 (t, 3H).

Step 4. Preparation of ethyl 7,7-difluoro-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P25)**

To a reaction mixture of **C47** (0.416 g, 1.20 mmol) in DCM (5 mL) was added HCl in dioxane (1.76 g, 48.2 mmol) and then stirred at room temperature for 2.5 h. The reaction mixture was concentrated *in vacuo* to provide **P25** (295 mg, crude) as a light-yellow solid. The solid was used directly in the next step without further purification. (LC/MS) m/z (M+H)$^+$ = 246.1. ^{1}H NMR (400 MHz, CD_3OD) δ 4.55 (t, 2H), 4.40 (q, 2H), 4.15 – 4.02 (m, 5H), 1.39 (t, 3H).

Preparation 26

rac-Ethyl (4*R*,8*S*)-1-methyl-1,4,5,7,8,9-hexahydro-4,8-epiminooxocino[5,4-*c*]pyrazole-3-carboxylate hydrochloride **(P26)**



Step 1. Preparation of *rac-tert*-butyl *(1R,5S)*-6-(2-ethoxy-2-oxoacetyl)-7-oxo-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate **(C49)**

The same procedure was followed from **Preparation 20, step 1** with *tert*-butyl 7-oxo-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (CAS: 280761-97-9; 1.80 g, 7.46 mmol) to provide **C49** (2.50 g, crude) as an orange oil, which was used directly in the next step without further purification.

Step 2. Preparation of *rac*-10-(*tert*-butyl) 3-ethyl (4*R*,8*S*)-1-methyl-1,4,5,7,8,9-hexahydro-4,8-epiminooxocino[5,4-*c*]pyrazole-3,10-dicarboxylate **(C50)** and *rac*-10-(*tert*-butyl) 3-ethyl (4*R*,8*S*)-2-methyl-2,4,5,7,8,9-hexahydro-4,8-epiminooxocino[5,4-*c*]pyrazole-3,10-dicarboxylate **(C51)**

The reaction was conducted in two batches and then combined. A suspension of **C49** (2.50 g, 7.32 mmol) and methylhydrazine dihydrochloride (CAS: 55330-60-4; 0.871 g, 7.32 mmol) in EtOH (40 mL) and pyridine (2.55 g, 32.2 mmol) was stirred at room temperature for 3 h to form the first batch. The reaction mixture of the first batch was checked by LCMS, which showed the major isomer of **C50** [LC/MS) m/z $(M+H)^+$ = 352.3 at 0.827 min retention time (analytical LCMS conditions: Chromolith Flash Reverse Phase-18e 25-3mm column; Mobile Phase A: 1.5 mL/ 4 L TFA in H_2O/ Mobile Phase B: 0.75 mL/ 4 L TFA in ACN, gradient 5-95% of Mobile Phase B over 0.7 min then held at 95% of Mobile Phase B for 0.4 min; flow rate: 1.5 mL/ min column temperature: 50 °C)] and the minor isomer of **C51** [LC/MS) m/z $(M+H)^+$ = 352.3 at 0.880 min retention time (analytical LCMS conditions: Chromolith Flash Reverse Phase-18e 25-3mm column; Mobile Phase A: 1.5 mL/ 4 L TFA in H_2O/ Mobile Phase B: 0.75 mL/ 4 L TFA in ACN, gradient 5-95% of Mobile Phase B over 0.7 min then held at 95% of Mobile Phase B for 0.4 min; flow rate: 1.5 mL/ min column temperature: 50 °C)].

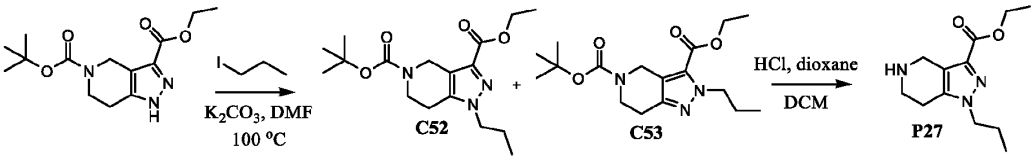
The second batch of the same reaction was conducted with **C49** (0.200 g, 0.586 mmol). The two batches were combined, concentrated in vacuo, and purified by column chromatography (silica gel, 0-50% EtOAc: PE) to provide **C50** (0.750 g, 27.0% yield) as a yellow solid. (LC/MS) m/z $(M+H)^+$ = 352.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 – 5.30 (m, 1H), 4.53 – 4.27 (m, 3H), 3.91 – 3.64 (m, 7H), 3.21 – 2.92 (m, 1H), 2.71 – 2.59 (m, 1H), 1.51 – 1.30 (m, 12H).

Step 3. Preparation of *rac*-ethyl (4*R*,8*S*)-1-methyl-1,4,5,7,8,9-hexahydro-4,8-epiminooxocino[5,4-*c*]pyrazole-3-carboxylate hydrochloride **(P26)**

To a solution of **C50** (0.750 g, 2.14 mmol) in DCM (5 mL) was added 2M HCl in dioxane (0.390 g, 10.7 mmol). The reaction mixture was stirred at room temperature for 2 h and then concentrated *in vacuo*. The residue was dissolved in DCM (5 mL) and then concentrated *in vacuo* (2x) to provide **P26** (0.675 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (s, 1H), 9.85 (s, 1H), 5.07 (s, 1H), 4.45 – 4.20 (m, 4H), 4.01 – 3.84 (m, 5H), 3.82 – 3.73 (m, 1H), 3.66 – 3.55 (m, 1H), 2.98 – 2.86 (m, 1H), 1.38 (t, 3H).

Preparation 27

Ethyl 1-propyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P27)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-propyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C52)** and 2-((3-(ethoxycarbonyl)-2-propyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C53)**

To a solution of 5-(*tert*-butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 0.81 g, 4.7 mmol) and 1-iodopropane (1.0 g, 3.4 mmol) in DMF (13 mL) was added K_2CO_3 (0.94 g, 6.7 mmol). The reaction mixture was stirred at 100 °C for 4 h, cooled to room temperature, and diluted with (1:1) EtOAc: H_2O (50 mL). The aqueous layer was extracted with EtOAc (3 x 25 mL). The combined organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-39% EtOAc: PE) to provide **C53** (0.48 g, 42% yield) as a white solid and **C52** (0.38 g, 33% yield) as a white solid.

C52: (LC/MS) m/z $(M+H)^+$ = 338.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.61 (s, 2H), 4.39 (q, 2H), 4.03 (t, 2H), 3.76 – 3.67 (m, 2H), 2.73 – 2.63 (m, 2H), 1.92 – 1.80 (m, 2H), 1.48 (s, 9H), 1.39 (t, 3H), 0.91 (t, 3H).

C53: (LC/MS) m/z $(M+H)^+$ = 338.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 – 4.56 (m, 2H), 4.49 – 4.43 (m, 2H), 4.33 (q, 2H), 3.68 (s, 2H), 2.74 (s, 2H), 1.90 – 1.78 (m, 2H), 1.49 (s, 9H), 1.39 (t, 3H), 0.92 (t, 3H).

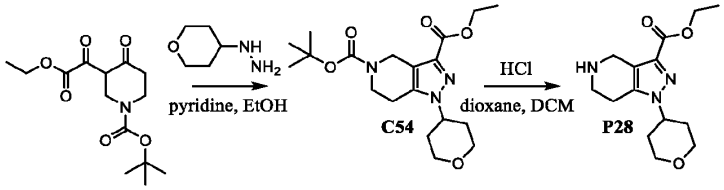
Step 2. Preparation of ethyl 1-propyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P27)**

To a reaction mixture of **C52** (0.370 g, 1.10 mmol) in DCM (3 mL) was added 2M HCl in dioxane (0.400 g, 11.0 mmol) and then stirred at room temperature for 1 h and 40 min. The reaction mixture was concentrated *in vacuo* to provide **P27** (0.300 g, crude) as a white solid.

The solid was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.54 (s, 2H), 4.25 (q, 2H), 4.19 (s, 2H), 4.06 (t, 2H), 3.40 – 3.35 (m, 2H), 2.97 (t, 2H), 1.80 – 1.68 (m, 2H), 1.27 (t, 3H), 0.82 (t, 3H).

Preparation 28

Ethyl 1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P28)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-(tetrahydro-2*H*-pyran-4-yl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C54)**

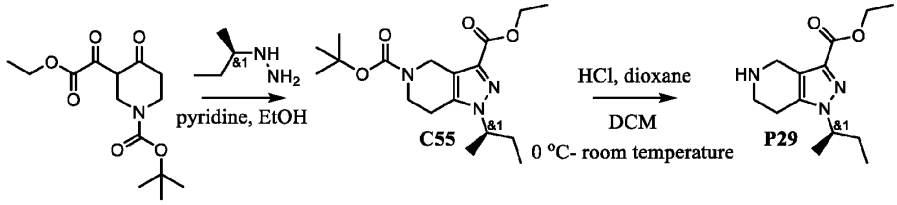
The same procedure was followed from **Preparation 2, step 1** with *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 0.500 g, 1.67 mmol) and (tetrahydro-2*H*-pyran-4-yl)hydrazine hydrochloride (0.255 g, 1.67 mmol). The residue was purified by column chromatography (silica gel, 0-40% THF: PE) to provide **C54** (0.492 g, 77.6% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 380.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.60 (s, 2H), 4.38 (q, 2H), 4.31 – 4.21 (m, 1H), 4.15 – 4.07 (m, 2H), 3.77 – 3.68 (m, 2H), 3.54 – 3.44 (m, 2H), 2.73 (t, 2H), 2.41 – 2.25 (m, 2H), 1.89 – 1.80 (m, 2H), 1.51 – 1.40 (m, 9H), 1.38 (t, 3H).

Step 2. Preparation of ethyl 1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P28)**

To a solution of **C54** (0.470 g, 1.24 mmol) in DCM (10 mL) was added 2M HCl in dioxane (0.973 g, 26.7 mmol). The reaction mixture was stirred at room temperature for 4 h then concentrated *in vacuo* to provide **P28** (0.370 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 280.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.37 (s, 1H), 4.56 – 4.45 (m, 1H), 4.33 – 4.19 (m, 4H), 4.03 – 3.93 (m, 2H), 3.52 – 3.41 (m, 4H), 3.04 (t, 2H), 2.07 – 1.92 (m, 2H), 1.86 – 1.77 (m, 2H), 1.29 (t, 3H).

Preparation 29

rac-Ethyl (*R*)-1-(*sec*-butyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P29)**



Step 1. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1-(*sec*-butyl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C55)**

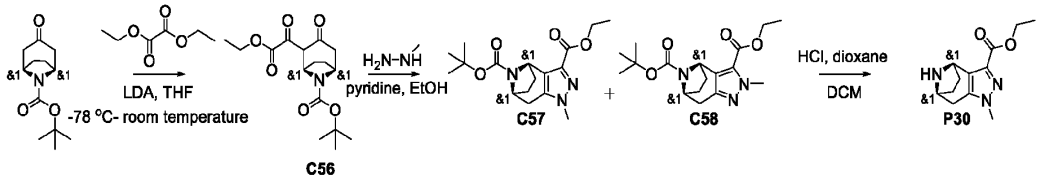
The same procedure was followed from **Preparation 2, step 1** with *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 0.400 g, 1.34 mmol) and *sec*-butylhydrazine dihydrochloride (CAS: 1177361-36-2, 0.215 g, 1.34 mmol). The residue was purified by column chromatography (silica gel, 50% EtOAc: PE) to provide **C55** (0.382 g, 81.3% yield) as a gum. (LC/MS) m/z $(M+H)^+$ = 352.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 4.53 – 4.40 (m, 2H), 4.30 – 4.17 (m, 3H), 3.68 – 3.54 (m, 2H), 2.71 (q, 2H), 1.87 – 1.66 (m, 2H), 1.41 (s, 9H), 1.37 (d, 3H), 1.29 (t, 3H), 0.69 (t, 3H).

Step 2. Preparation of *rac*-ethyl (*R*)-1-(*sec*-butyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P29)**

At 0 °C, to a solution of **C55** (0.382 g, 1.09 mmol) in DCM (2 mL) was added HCl in dioxane (4 mL). The reaction mixture was stirred at room temperature for 16 h then concentrated *in vacuo* to provide **P29** (0.245 g, crude) as a solid. The solid was used directly in the next step without further purification.

Preparation 30

rac-Ethyl (4*R*,7*S*)-1-methyl-1,4,5,6,7,8-hexahydro-4,7-epiminocyclohepta[*c*]pyrazole-3-carboxylate **(P30)**



Step 1. Preparation of *rac-tert*-butyl (1*R*,5*S*)-2-(2-ethoxy-2-oxoacetyl)-3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate **(C56)**

The same procedure was followed from **Preparation 20, step 1**, with tert-butyl (1R,5S)-8-oxo-3-azabicyclo[3.2.1]octane-3-carboxylate (CAS: 637301-19-0; 5.10 g, 22.6 mmol), with an additional purification added. The residue was purified by column chromatography (silica gel, 0-10% EtOAc: PE) to provide **C56** (4.69 g, 63.7% yield) as a yellow oil.

Step 2. Preparation of *rac*-9-(*tert*-butyl) 3-ethyl (4*R*,7*S*)-1-methyl-1,4,5,6,7,8-hexahydro-4,7-epiminocyclohepta[*c*]pyrazole-3,9-dicarboxylate **(C57)** and *rac*-9-(*tert*-butyl) 3-ethyl (4*R*,7*S*)-2-methyl-2,4,5,6,7,8-hexahydro-4,7-epiminocyclohepta[*c*]pyrazole-3,9-dicarboxylate **(C58)**

The same procedure was followed from **Preparation 2, step 1** with **C56** (4.69 g, 14.4 mmol) and methylhydrazine sulfate (CAS: 302-15-8, 2.08 g, 14.4 mmol). The reaction mixture was checked by LCMS, which showed the major isomer of **C57** [LC/MS) m/z $(M+H)^+$ = 336.2 at 0.846 min retention time (analytical LCMS conditions: Chromolith Flash Reverse Phase-18e 25-

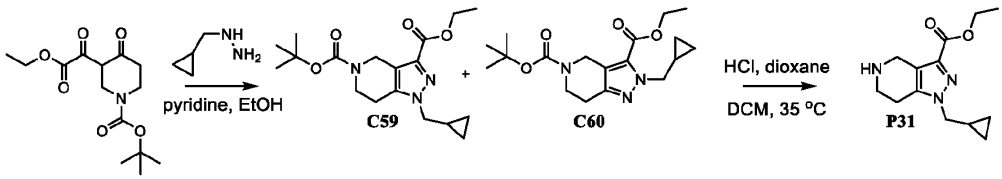
3mm column; Mobile Phase A: 1.5 mL/ 4 L TFA in H_2O/ Mobile Phase B: 0.75 mL/ 4 L TFA in ACN, gradient 5-95% of Mobile Phase B over 0.7 min then held at 95% of Mobile Phase B for 0.4 min; flow rate: 1.5 mL/ min; column temperature: 50 °C)] and the minor isomer of **C58** [LC/MS) m/z $(M+H)^+$ = 336.2 at 0.904 min retention time (analytical LCMS conditions: Chromolith Flash Reverse Phase-18e 25-3mm column; Mobile Phase A: 1.5 mL/ 4 L TFA in H_2O/ Mobile Phase B: 0.75 mL/ 4 L TFA in ACN, gradient 5-95% of Mobile Phase B over 0.7 min then held at 95% of Mobile Phase B for 0.4 min; flow rate: 1.5 mL/ min; column temperature: 50 °C)]. The purification was altered. The residue was purified by column chromatography (silica gel, 0-50% THF: PE) to provide **C57** (1.40 g, 29.0% yield) as a light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 – 5.33 (m, 1H), 4.64 – 4.35 (m, 3H), 3.77 (s, 3H), 3.29 – 3.08 (m, 1H), 2.41 – 2.23 (m, 2H), 2.21 – 2.10 (m, 1H), 1.93 – 1.85 (m, 1H), 1.55 – 1.48 (m, 1H), 1.44 – 1.35 (m, 12H).

Step 3. Preparation of ethyl 1-methyl-1,4,5,6,7,8-hexahydro-4,7-epiminocyclohepta[*c*]pyrazole-3-carboxylate **(P30)**

To a solution of **C57** (0.240 g, 0.716 mmol) in DCM (1 mL), 2M HCl in dioxane (3 mL) was added. The reaction mixture was stirred at room temperature for 2.5 h and then concentrated *in vacuo* to provide **P30** (0.168 g, crude) as a grey solid. The solid was used directly in the next step without further purification.

Preparation 31

Ethyl 1-(cyclopropylmethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-c]pyridine-3-carboxylate **(P31)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-(cyclopropylmethyl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C59)** and 2-((2-(cyclopropylmethyl)-3-(ethoxycarbonyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C60)**

The same procedure was followed from **Preparation 2, step 1** with *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 2.00 g, 6.68 mmol) and (cyclopropylmethyl)hydrazine hydrochloride (CAS: 1181457-83-9, 0.655 g, 5.35 mmol). The residue was purified by column chromatography (silica gel, 0-60% EtOAc: PE) to provide an impure **C60** (0.800 g) as a yellow oil and **C59** (0.940 g, 40.3% yield) as a light-brown solid. **C60** (0.800 g) was repurified by column chromatography (silica gel, 0-10% EtOAc: DCM) to provide **C60** (0.450 g, 19.3% yield) as a grey gum.

C59: (LC/MS) m/z $(M+H)^+$ = 350.1; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 4.49 (s, 2H), 4.26 (q, 2H), 3.96 (d, 2H), 3.61 (t, 2H), 2.73 (t, 2H), 1.44 – 1.40 (m, 9H), 1.29 (t, 3H), 1.24 – 1.16 (m, 1H), 0.54 – 0.47 (m, 2H), 0.37 – 0.31 (m, 2H).

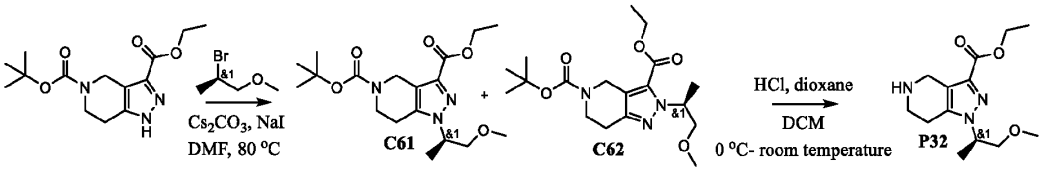
C60: (LC/MS) m/z $(M+H)^+$ = 350.0; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62 (s, 2H), 4.41 – 4.30 (m, 4H), 3.76 – 3.61 (m, 2H), 2.81 – 2.71 (m, 2H), 1.50 – 1.46 (m, 9H), 1.42 - 1.30 (m, 4H), 0.54 – 0.47 (m, 2H), 0.43 – 0.37 (m, 2H).

Step 2. Preparation of ethyl 1-(cyclopropylmethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P31)**

To a solution of **C59** (0.200 g, 0.572 mmol) in DCM (0.5 mL), 2M HCl in dioxane (2.0 mL) was added. The reaction mixture was stirred at 35 °C for 3 h and then concentrated *in vacuo* to provide **P31** (0.143 g, crude) as a grey solid. The solid was used directly in the next step without further purification.

Preparation 32

rac-Ethyl (*R*)-1-(1-methoxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P32)**



Step 1. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1-(1-methoxypropan-2-yl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C61)** and *rac*-(*R*)-2-((3-(ethoxycarbonyl)-2-(1-methoxypropan-2-yl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C62)**

The reaction was conducted in two batches then combined for purification. A solution of *rac*-(*R*)-2-bromo-1-methoxypropane (CAS: 22461-48-9; 0.829 g, 5.42 mmol), 5-(*tert*-butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 0.800 g, 2.71 mmol), Cs_2CO_3 (1.77 g, 5.42 mmol) and NaI (40.6 mg, 0.271 mmol) in DMF (13.5 mL) was stirred at 80 °C for 16 h to form the first batch.

The second batch of the same reaction was conducted with 5-(*tert*-butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 0.100 g, 0.339 mmol). The two batches were combined then diluted with H_2O (20 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layer was dried Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-50% EtOAc: PE) to provide **C62** (0.630 g, 56.2% yield) as an oil and **C61** (0.430 g, 38.4% yield) as an oil.

C62: (LC/MS) m/z $(M+H)^+$ = 368.2; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 – 5.60 (m, 1H), 4.68 – 4.55 (m, 2H), 4.33 (q, 2H), 3.85 (t, 1H), 3.74 – 3.63 (m, 2H), 3.55 (dd, 1H), 3.31 (s, 3H), 2.79 – 2.71 (m, 2H), 1.48 (s, 9H), 1.45 – 1.36 (m, 6H).

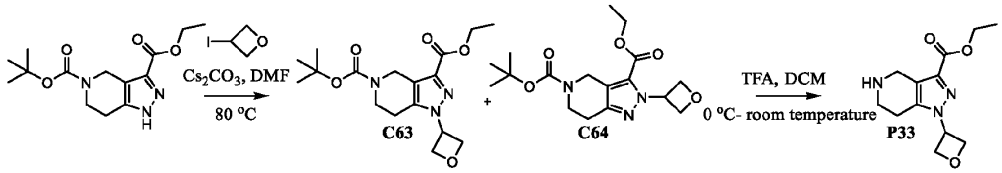
C61: (LC/MS) m/z $(M+H)^+$ = 368.2; ^1H NMR (400 MHz, $CDCl_3$) δ 4.60 (s, 2H), 4.43 – 4.33 (m, 3H), 3.82 – 3.75 (m, 1H), 3.73 – 3.66 (m, 2H), 3.58 (dd, 1H), 3.24 (s, 3H), 2.83 – 2.62 (m, 2H), 1.52 – 1.46 (m, 12H), 1.38 (t, 3H).

Step 2. Preparation of *rac*-ethyl (*R*)-1-(1-methoxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P32)**

At 0 °C, to a suspension of **C61** (0.430 g, 1.17 mmol) in DCM (2 mL) was added HCl in dioxane (8 mL) in batches. The reaction mixture was stirred at room temperature for 2 h then concentrated *in vacuo* to provide **P32** (0.356 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 268.1. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 9.28 – 9.05 (m, 2H), 4.66 – 4.55 (m, 1H), 4.36 – 4.13 (m, 4H), 3.67 – 3.57 (m, 1H), 3.55 – 3.51 (m, 1H), 3.48 – 3.38 (m, 2H), 3.18 (s, 3H), 3.08 – 2.86 (m, 2H), 1.36 (d, 3H), 1.29 (t, 3H).

Preparation 33

Ethyl 1-(oxetan-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate trifluoroacetate **(P33)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-(oxetan-3-yl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C63)** and 2-((3-(ethoxycarbonyl)-2-(oxetan-3-yl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C64)**

The reaction was conducted in two batches then combined for purification. To a solution of 5-(*tert*-butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 0.600 g, 2.03 mmol) in DMF (10 mL) was added 3-iodooxetane (CAS: 26272-85-5; 0.748 g, 4.06 mmol) and Cs_2CO_3 (1.32 g, 4.06 mmol) then stirred at 80 °C for 16 h to form the first batch.

The second batch of the same reaction conducted with 5-(*tert*-butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 0.100 g, 0.339 mmol) then the two batches were combined then diluted in ice H_2O (40 mL). The diluted reaction mixture was extracted with EtOAc (3 x 10 mL). The combined organic layer was washed with brine (2 x 10 mL) then concentrated *in vacuo*. The residue was purified by column

chromatography (silica gel, 0-80% EtOAc: PE) to provide **C63** (0.180 g, 25.2% yield) as an oil and **C64** (0.288 g, 40.3% yield) as an oil.

C63 (Lot-001): (LC/MS) m/z $(M+H)^+$ = 352.1; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 5.61 – 5.51 (m, 1H), 4.89 (d, 4H), 4.49 (s, 2H), 4.33 – 4.24 (m, 2H), 3.58 (t, 2H), 2.68 (t, 2H), 1.41 (s, 9H), 1.31 (t, 3H).

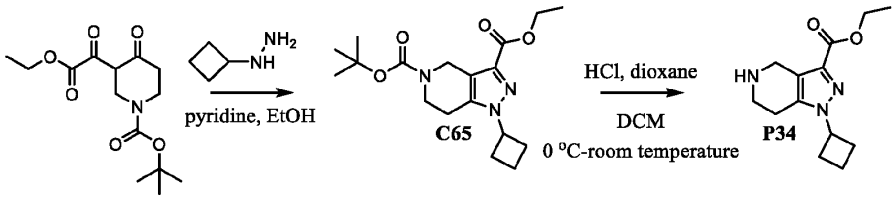
C64: (LC/MS) m/z (M-*tert*-butyl group)$^+$ = 296.1; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 6.08 – 5.95 (m, 1H), 4.97 – 4.84 (m, 4H), 4.56 – 4.50 (m, 2H), 4.28 (q, 2H), 3.62 (t, 2H), 2.70 (t, 2H), 1.42 (s, 9H), 1.30 (t, 3H).

Step 2. Preparation of ethyl 1-(oxetan-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate trifluoroacetate **(P33)**

At 0 °C, to a suspension of **C63** (0.180 g, 0.512 mmol) in DCM (3 mL) was added TFA (3 mL). The reaction mixture was stirred at room temperature for 3 h and then concentrated *in vacuo* to provide **P33** (0.187 g, crude) as a gum. The gum was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 252.3. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.18 – 8.94 (m, 2H), 5.69 – 5.58 (m, 1H), 4.98 – 4.82 (m, 4H), 4.37 – 4.23 (m, 4H), 3.44 – 3.35 (m, 2H), 3.04 – 2.91 (m, 2H), 1.35 – 1.26 (m, 3H).

Preparation 34

Ethyl 1-(cyclobutylmethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P34)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1-(cyclobutylmethyl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C65)**

The same procedure was followed from **Preparation 2, step 1** with *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 0.400 g, 1.34 mmol) and 1-cyclobutylhydrazine hydrochloride (CAS: 158001-21-9, 0.164 g, 1.34 mmol) to provide **C65** (0.280 g, 15.0% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 350.2. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 4.90 – 4.75 (m, 1H), 4.48 (s, 2H), 4.28 (q, 2H), 3.60 (t, 2H), 2.73 – 2.66 (m, 2H), 2.40 – 2.30 (m, 4H), 1.87 – 1.74 (m, 2H), 1.46 – 1.35 (m, 9H), 1.30 (t, 3H).

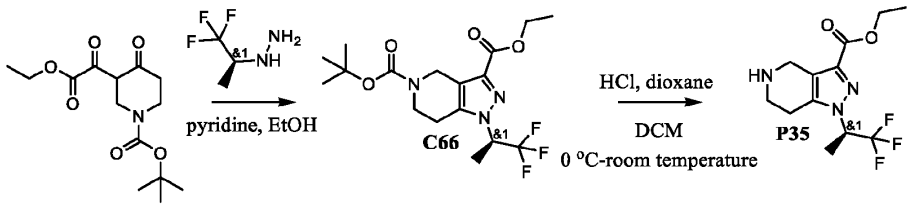
Step 2. Preparation of ethyl 1-(cyclobutylmethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P34)**

At 0 °C, HCl was added to a suspension of **C65** (0.280 g, 0.801 mmol) in DCM (5 mL) in dioxane (10 mL). The reaction mixture was stirred at room temperature for 3 h, concentrated *in*

vacuo, and then lyophilized to provide **P34** (0.150 g, crude) as a brown solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 250.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.37 (s, 2H), 4.94 – 4.80 (m, 1H), 4.29 (q, 2H), 4.21 (s, 2H), 3.42 – 3.36 (m, 2H), 2.95 (t, 2H), 2.48 – 2.44 (m, 1H), 2.41 – 2.31 (m, 2H), 1.87 – 1.75 (m, 2H), 1.30 (t, 3H).

Preparation 35

rac-Ethyl (*R*)-1-(1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P35)**



Step 1. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1-(1,1,1-trifluoropropan-2-yl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C66)**

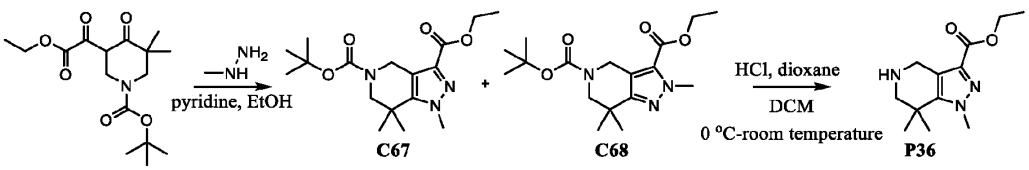
To a solution of *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxopiperidine-1-carboxylate (CAS: 518990-24-4; 0.400 g, 1.34 mmol) and (1,1,1-trifluoropropan-2-yl)hydrazine hydrochloride (CAS: 1453472-98-4; 0.269 g, 1.34 mmol) in EtOH (7 mL) was added pyridine (0.465 g, 5.88 mmol). The reaction mixture was stirred at room temperature for 5 h and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-25% EtOAc: PE) to provide **C66** (0.415 g, 79.3% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 392.2. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 5.47 – 5.35 (m, 1H), 4.60 – 4.38 (m, 2H), 4.29 (q, 2H), 3.78 – 3.67 (m, 1H), 3.55 – 3.46 (m, 1H), 2.92 – 2.81 (m, 1H), 2.69 – 2.56 (m, 1H), 1.67 (d, 3H), 1.41 (s, 9H), 1.30 (t, 3H).

Step 2. Preparation of *rac*-ethyl (*R*)-1-(1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P35)**

At 0 °C, to a suspension of **C66** (0.415 g, 1.06 mmol) in DCM (4 mL) was added HCl in dioxane (8 mL) in batches. The reaction mixture was stirred at room temperature for 16 h then concentrated *in vacuo* to provide **P35** (0.306 g, crude) as a yellow solid. The solid was used directly in the next step without further purification.

Preparation 36

Ethyl 1,7,7-trimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P36)**



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 1,7,7-trimethyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C67)** and 2-((3-(ethoxycarbonyl)-2,7,7-trimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C68)**

The same procedure was followed from **Preparation 2, step 1** with *tert*-butyl 5-(2-ethoxy-2-oxoacetyl)-3,3-dimethyl-4-oxopiperidine-1-carboxylate (CAS: 2171295-98-8, 1.28 g, 3.91 mmol) and methylhydrazine (CAS: 60-34-4, 1.08 g, 9.38 mmol) to provide **C68** (0.563 g, 42.7% yield) as a light-yellow gum and **C67** (0.160 g, 12.1% yield) as a light-yellow gum.

C67: (LC/MS) m/z $(M+H)^+$ = 338.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 – 4.54 (m, 2H), 4.44 – 4.30 (m, 2H), 4.00 – 3.92 (m, 3H), 3.45 – 3.34 (m, 2H), 1.51 – 1.45 (m, 9H), 1.41 – 1.35 (m, 3H), 1.34 – 1.29 (m, 6H).

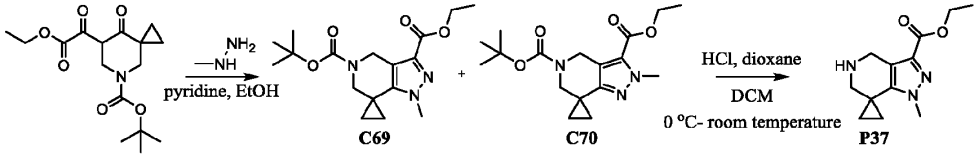
C68: (LC/MS) m/z $(M+H)^+$ = 338.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 – 4.56 (m, 2H), 4.38 – 4.26 (m, 2H), 4.16 – 4.05 (m, 3H), 3.45 – 3.32 (m, 2H), 1.49 – 1.46 (m, 9H), 1.37 (t, 3H), 1.28 – 1.24 (m, 6H).

Step 2. Preparation of ethyl 1,7,7-trimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P36)**

At 0 °C, to a suspension of **C67** (0.130 g, 0.385 mmol) in DCM (3 mL) was added HCl in dioxane (3 mL). The reaction mixture was stirred at room temperature for 2 h and then concentrated *in vacuo* to provide **P36** (0.110 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 238.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.58 (s, 2H), 4.27 (q, 2H), 4.18 (s, 2H), 3.98 (s, 3H), 3.21 – 3.16 (m, 2H), 1.42 (s, 6H), 1.31 – 1.22 (m, 3H).

Preparation 37

Ethyl 1'-methyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxylate hydrochloride **(P37)**



Step 1. Preparation of 5'-(*tert*-butyl) 3'-ethyl 1'-methyl-1',4'-dihydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3',5'(6'*H*)-dicarboxylate **(C69)** and 2-((3'-(ethoxycarbonyl)-2'-methyl-2',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-5'-carbonyl)oxy)-2-methylpropan-1-ylium **(C70)**

The same procedure was followed from **Preparation 2, step 1** with *tert*-butyl 7-(2-ethoxy-2-oxoacetyl)-8-oxo-5-azaspiro[2.5]octane-5-carboxylate (CAS: 2494304-89-9; 0.620 g, 1.91 mmol) and methylhydrazine sulfate (CAS: 302-15-8, 0.302 g, 2.10 mmol). The purification was altered. The residue was purified by column chromatography (silica gel, 0-30% THF: PE) to

provide **C70** (0.327 g, 51.2% yield) as a white solid and **C69** (0.290 g, 45.4% yield) as a white gum.

C69: (LC/MS) m/z $(M+H)^+$ = 336.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (s, 2H), 4.39 (q, 2H), 3.74 (s, 3H), 3.44 (s, 2H), 1.48 (s, 9H), 1.39 (t, 3H), 1.31 (t, 2H), 1.08 – 0.94 (m, 2H).

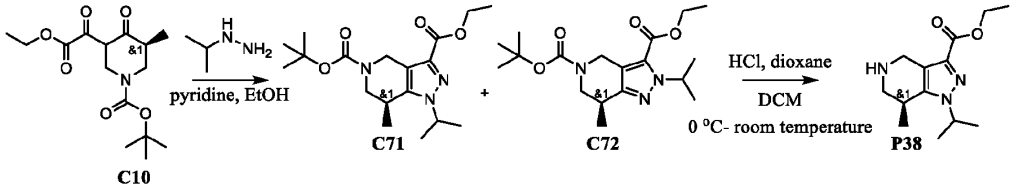
C70: (LC/MS) m/z $(M+H)^+$ = 336.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 – 4.65 (m, 2H), 4.34 (q, 2H), 4.08 (s, 3H), 3.53 – 3.47 (m, 2H), 1.48 (s, 9H), 1.39 (t, 3H), 1.12 (q, 2H), 0.97 – 0.86 (m, 2H).

Step 2. Preparation of ethyl 1'-methyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxylate hydrochloride **(P37)**

At 0 °C, to a suspension of **C69** (0.272 g, 0.811 mmol) in DCM (6 mL) was added HCl in dioxane (0.591 g, 16.2 mmol). The reaction mixture was stirred at room temperature for 3 h then concentrated *in vacuo* to provide **P37** (0.219 g, crude) as a white solid. The solid was used directly in the next step without further purification.

Preparation 38

rac-Ethyl (*R*)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P38)**



Step 1. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C71)** and *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-2-isopropyl-7-methyl-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C72)**

The same procedure was followed from **Preparation 2, step 1** with **C10** (3.00 g, 9.57 mmol) and isopropylhydrazine hydrochloride (CAS: 16726-41-3, 1.06 g, 9.57 mmol). The purification was altered. The residue was purified by reverse phase HPLC (Sunfire C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O (0.05% NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, Mobile Phase B: 42 to 82% over 9.0 min, 100% of Mobile Phase B hold 2.0 min, flow rate= 30 mL/min) to provide **C71** (1.80 g, 53.5% yield) as a pale yellow solid and **C72** (33.9 mg, 1.01% yield) as a pale yellow solid.

C71: (LC/MS) m/z $(M+H)^+$ = 352.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (dd, 1H), 4.46 – 4.31 (m, 3H), 4.13 (dd, 2H), 3.20 – 3.04 (m, 1H), 2.99 – 2.89 (m, 1H), 1.54 (d, 3H), 1.51 – 1.45 (m, 12H), 1.36 (t, 3H), 1.23 (d, 3H).

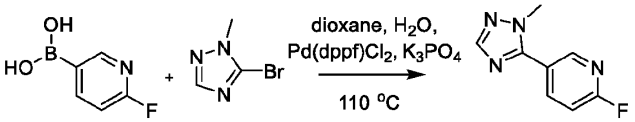
C72: (LC/MS) m/z $(M+H)^+$ = 352.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 – 5.44 (m, 1H), 4.69 – 4.45 (m, 2H), 4.32 (q, 2H), 3.90 – 3.61 (m, 1H), 3.41 – 3.13 (m, 1H), 3.02 – 2.92 (m, 1H), 1.51 – 1.44 (m, 15H), 1.38 (t, 3H), 1.26 (d, 3H).

Step 2. Preparation of *rac*-ethyl (*R*)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P38)**

At 0 °C, to a suspension of **C71** (0.200 g, 0.569 mmol) in DCM (1 mL) was added HCl in dioxane (4 mL). The reaction mixture was stirred at room temperature for 2 h then concentrated *in vacuo* to provide **P38** (0.180 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 252.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.98 – 9.83 (m, 1H), 9.34 – 9.25 (m, 1H), 4.67 – 4.54 (m, 1H), 4.33 – 4.05 (m, 4H), 3.43 – 3.26 (m, 3H), 1.45 – 1.40 (m, 3H), 1.39 – 1.33 (m, 6H), 1.32 – 1.26 (m, 3H).

Preparation 39

2-Fluoro-5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridine **(P39)**



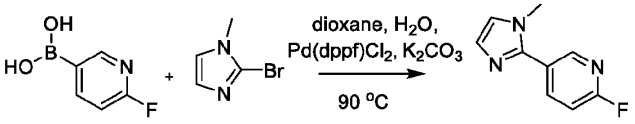
P39

Step 1. Preparation of 2-fluoro-5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridine **(P39)**

To a suspension of (6-fluoropyridin-3-yl)boronic acid (CAS: 351019-18-6; 1.10 g, 7.81 mmol) and 5-bromo-1-methyl-1*H*-1,2,4-triazole (CAS: 16681-72-4; 1.52 g, 9.37 mmol) in dioxane (10 mL) and H_2O (2 mL) was added $Pd(dppf)Cl_2$ (0.457 g, 0.625 mmol) and K_3PO_4 (4.97 g, 23.4 mmol). The reaction mixture was degassed with nitrogen gas, then stirred at 110 °C for 4 h and purified by column chromatography (silica gel, 0-40% EtOAc: PE) to provide **P39** (1.20 g, 86.3% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 179.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.67 – 8.62 (m, 1H), 8.42 – 8.34 (m, 1H), 8.05 (s, 1H), 7.40 (dd, 1H), 3.97 (s, 3H).

Preparation 40

2-Fluoro-5-(1-methyl-1*H*-imidazol-2-yl)pyridine **(P40)**



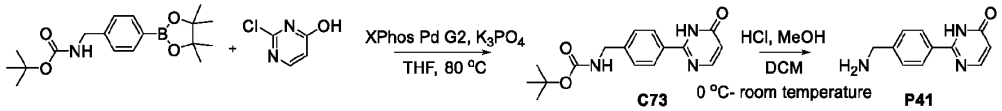
P40

Step 1. Preparation of 2-fluoro-5-(1-methyl-1*H*-imidazol-2-yl)pyridine **(P40)**

Under nitrogen gas, the reaction mixture of 2-bromo-1-methyl-1*H*-imidazole (0.700 g, 4.35 mmol), (6-fluoropyridin-3-yl)boronic acid (1.20 g, 8.70 mmol) and $Pd(dppf)Cl_2$ (0.178 g, 0.217 mmol) suspended in dioxane (10 mL) and H_2O (2 mL) was stirred at 90 °C for 1 h. The reaction mixture was extracted with EtOAc, and then the organic layer was concentrated *in vacuo*. The residue was dissolved in DCM and then purified by column chromatography (silica gel, 0-10% MeOH: DCM) to provide **P40** (0.688 g, 89.3% yield) as an orange oil. (LC/MS) m/z $(M+H)^+$ = 178.1.

Preparation 41

2-(4-(Aminomethyl)phenyl)pyrimidin-4(3*H*)-one hydrochloride **(P41)**



Step 1. Preparation of *tert*-butyl (4-(6-oxo-1,6-dihydropyrimidin-2-yl)benzyl)carbamate **(C73)**

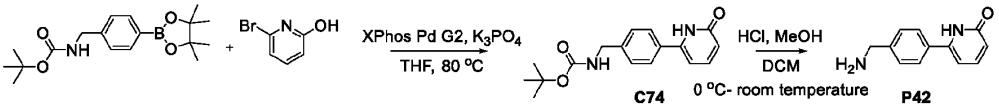
To a solution of 2-chloropyrimidin-4-ol (CAS: 55873-09-1; 0.100 g, 0.766 mmol) and *tert*-butyl (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)carbamate (CAS: 330794-35-9; 0.255 g, 0.766 mmol) in THF (7.7 mL) was added 2M K_3PO_4 (0.325 g, 1.53 mmol). The reaction mixture was degassed with nitrogen gas for 3 min, and then XPhos Pd G2 (60.3 mg, 0.0766 mmol) was added. The suspension was degassed with nitrogen gas for 3 min and then stirred at 80 °C for 4 h. The reaction solution was diluted with H_2O (10 mL) and then extracted with MeOH: DCM (1:10, 3 x 5 mL). The combined organic layer was dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE) to provide **C73** (0.115 g, 49.8% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 302.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.75 (br s, 1H), 8.16 – 7.92 (m, 3H), 7.51 – 7.44 (m, 1H), 7.36 (d, 2H), 6.36 – 6.24 (m, 1H), 4.18 (d, 2H), 1.39 (s, 9H).

Step 2. Preparation of 2-(4-(aminomethyl)phenyl)pyrimidin-4(3*H*)-one hydrochloride **(P41)**

At 0 °C, to a stirred solution of **C73** (0.115 g, 0.382 mmol) in DCM (1 mL) was added HCl in MeOH (3 mL). The reaction mixture was stirred at room temperature for 2 h and then concentrated *in vacuo* to provide **P41** (91.0 mg, crude) as a white solid. The solid was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 11.05 – 10.97 (m, 1H), 10.88 – 10.81 (m, 1H), 8.60 - 8.47 (m, 2H), 8.17 – 8.08 (m, 2H), 7.66 – 7.61 (m, 2H), 7.39 (dd, 1H), 6.40 – 6.36 (m, 1H), 5.46 – 5.42 (m, 1H), 4.10 (q, 2H).

Preparation 42

6-(4-(Aminomethyl)phenyl)pyridin-2(1*H*)-one hydrochloride **(P42)**



Step 1. Preparation of *tert*-butyl (4-(6-oxo-1,6-dihydropyridin-2-yl)benzyl)carbamate **(C74)**

To a solution of 6-bromopyridin-2-ol (CAS: 27992-32-1; 0.100 g, 0.575 mmol) and *tert*-butyl (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)carbamate (CAS: 330794-35-9; 0.192 g, 0.575 mmol) in THF (5.7 mL) was added 2M K_3PO_4 (0.244 g, 1.15 mmol). The reaction mixture was degassed with nitrogen gas for 3 min, then XPhos Pd G2 (45.2 mg, 0.0575 mmol) was added. The suspension was degassed with nitrogen gas for 3 min and then stirred at 80 °C

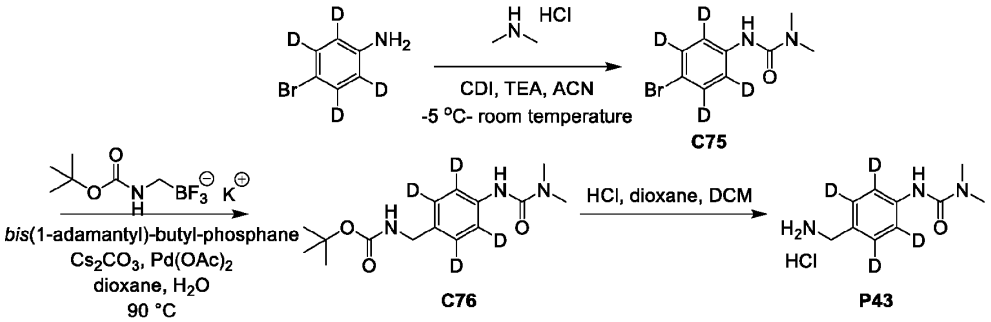
for 4 h. The reaction solution was diluted with H_2O (10 mL) and then extracted with EtOAc (3 x 5 mL). The combined organic layer was dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE) to provide **C74** (0.110 g, 63.7% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 301.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 11.71 (br s, 1H), 7.73 (d, 2H), 7.58 – 7.51 (m, 1H), 7.49 – 7.44 (m, 1H), 7.33 (d, 2H), 6.71 – 6.57 (m, 1H), 6.37 (d, 1H), 4.18 (d, 2H), 1.41 (s, 9H).

Step 2. Preparation of 6-(4-(aminomethyl)phenyl)pyridin-2(1*H*)-one hydrochloride **(P42)**

At 0 °C, to a stirred solution of **C74** (0.110 g, 0.366 mmol) in DCM (1 mL) was added HCl in MeOH (3 mL). The reaction mixture was stirred at room temperature for 2 h and then concentrated *in vacuo* to provide **P42** (87.0 mg, crude) as a white solid. The solid was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 – 8.36 (m, 3H), 7.84 (d, 2H), 7.61 – 7.54 (m, 3H), 6.80 – 6.70 (m, 1H), 6.43 (d, 1H), 4.07 (q, 2H).

Preparation 43

3-(4-(Aminomethyl)phenyl-2,3,5,6-*d*$_4$)-1,1-dimethylurea hydrochloride **(P43)**



Step 1. Preparation of 3-(4-bromophenyl-2,3,5,6-d$_4$)-1,1-dimethylurea **(C75)**

To a solution of CDI (6.59 g, 40.6 mmol) in ACN (50 mL) was added 4-bromobenzen-2,3,5,6-d$_4$-amine (CAS: 61357-76-4; 5.50 g, 31.2 mmol) at (-5 to 5) °C. The reaction mixture was stirred from (0 to 5) °C for 3 h before TEA (6.32 g, 62.5 mmol) and dimethylamine hydrochloride (CAS: 506-59-2; 5.10 g, 62.5 mmol) were added slowly at (0 to 5) °C. The reaction mixture was warmed to room temperature and stirred for 16 h. The suspension was poured into H_2O (100 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with brine (200 mL), dried over MgSO4, and concentrated *in vacuo*. The residue was slurried with MTBE: DCM (10:1, 100 mL) at room temperature for 3 h and then filtered. The filter cake was dried *in vacuo* and then collected to provide **C75** (6.10 g, 76.2% yield) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.40 (s, 1H), 2.91 (s, 6H).

Step 2. Preparation of *tert*-butyl (4-(3,3-dimethylureido)2,3,5,6-*d*$_4$-benzyl)carbamate **(C76)**

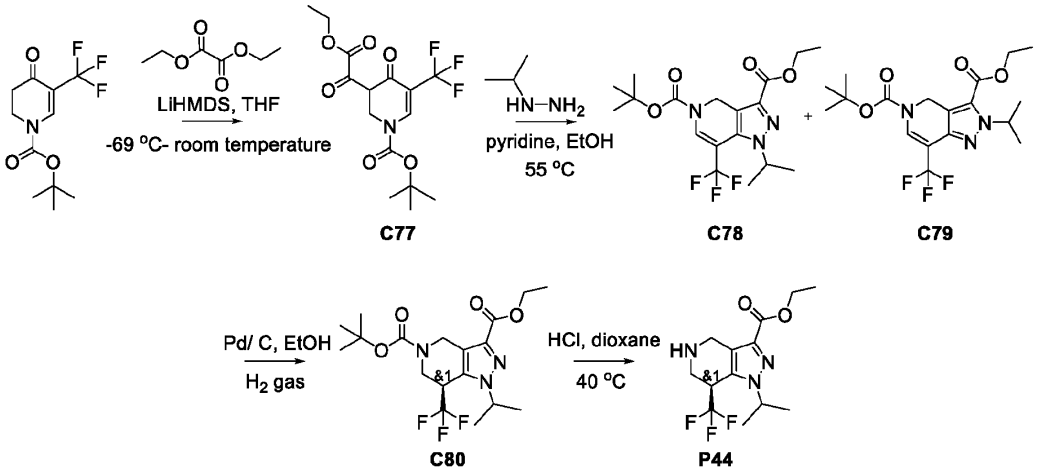
A reaction mixture of **C75** (3.0 g, 12 mmol), potassium [[(*tert*-butoxycarbonyl)amino]methyl]trifluoroborate (4.3 g, 18 mmol) and Cs_2CO_3 (7.9 g, 24 mmol) in H_2O (6 mL) and dioxane (40 mL) was degassed and purged with nitrogen gas 3 times. To the reaction mixture were added *bis*(1-adamantyl)-butyl-phosphane (0.87 g, 2.4 mmol) and $Pd(OAc)_2$ (0.27 g, 1.2 mmol). The suspension was degassed and purged with nitrogen gas 3 times again, then stirred at 90 °C for 16 h under nitrogen gas. The reaction mixture was cooled to room temperature and then poured into H_2O (50 mL) and filtered. The filtrate was extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with brine (100 mL), dried over MgSO4, and concentrated *in vacuo*. The residue was slurried with DCM (100 mL) at room temperature for 4 h and then filtered. The filter cake was dried *in vacuo* and then collected to provide **C76** (2.0 g, 30.% yield) as a light-yellow solid.

Step 3. Preparation of 3-(4-(aminomethyl)phenyl-2,3,5,6-d_4)-1,1-dimethylurea hydrochloride **(P43)**

To a solution of **C76** (2.0 g, 6.7 mmol) in DCM (30 mL) was added 2M HCl in dioxane (25 mL). The reaction mixture was stirred at room temperature for 16 h and then concentrated *in vacuo*. The residue was purified by reverse phase HPLC (Welch Xtimate C_{18} 250 mm x 50 mm x 10 µm column, Mobile Phase A: H_2O with HCl/ Mobile Phase B: ACN, 0 to 20% of Mobile Phase B over 20 min) then lyophilized to provide **P43** (1.1 g, 67% yield) as a white solid. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.43 (s, 1H), 8.37 (br s, 2H), 3.90 (q, 2H), 2.92 (s, 6H).

Preparation 44

rac-Ethyl (*R*)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P44)**



Step 1. Preparation of *tert*-butyl 3-(2-ethoxy-2-oxoacetyl)-4-oxo-5-(trifluoromethyl)-3,4-dihydropyridine-1(2*H*)-carboxylate **(C77)**

A yellow solution of 1M LiHMDS in THF (18.4 mL) was diluted with THF (10 mL) then cooled to -69 °C with a dry ice/ acetone bath. To the cooled solution was added *tert*-butyl 4-oxo-5-(trifluoromethyl)-3,4-dihydropyridine-1(2*H*)-carboxylate (CAS: 1667744-92-4; 4.07 g, 15.4 mmol) in THF (20 mL) dropwise over 15 min. The substrate flask was rinsed with THF (2 x 1 mL) and added to the reaction mixture. During the addition, the solution became a brownish-orange color. The reaction was stirred at -69 °C for 45 min after the addition.

A solution of diethyl oxalate (2.52 mL) in THF (5 mL) was added dropwise to the reaction mixture over 8 min. The source vial was rinsed with THF (1.5 mL), which was then added to the reaction mixture, which changed the solution to a brownish-orange color. The reaction mixture was stirred in the dry ice/acetone bath for another 7 min, then removed and replaced with an ice water bath. The reaction mixture was quenched with aqueous 2N HCl (21 mL), which changed the color of the suspension to an orange color. The suspension was diluted with H_2O and extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (1 x 20 mL, 2 x 10 mL). The organic layers were set aside. The aqueous layers were combined and washed with MTBE (3 x 20 mL). The combined organic layers were set aside. The aqueous layer was acidified with 6N HCl (~6.5 mL) to pH=1. The acidic aqueous layer was extracted with MTBE (2 x 40 mL). The combined organic layer from the acidic aqueous layer extraction was dried with Na_2SO_4, filtered, and concentrated *in vacuo*, then dried further by high vacuum to provide **C77** (1.52 g) as an orange-yellow residue.

The organic layers that were set aside were combined. The combined organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo* to give a deep orange oil. The oil was dissolved in MTBE (40 mL) and then washed with saturated $NaHCO_3$ solution (1 x 32 mL, 1 x 10 mL). The aqueous layers were combined and acidified with aqueous 6N HCl. The acidic aqueous layer was extracted with MTBE (30 mL) and then MTBE (20 mL). The organic layers were combined and then dried with Na_2SO_4, filtered, concentrated in vacuo, and dried further by high vacuum to provide **C77** (1.92 g) as an orange residue.

The two batches of products were combined to form **C77** (3.44 g) and then purified by column chromatography (silica gel, 0-85% EtOAc: heptane) to provide **C77** (2.32 g, 41.3% yield) as a yellow oil. (LC/MS) m/z $(M+H)^+$ = 366.5. 1H NMR (400 MHz, $CDCl_3$) δ 15.18 (s, 1H), 8.28 (s, 1H), 5.03 (s, 2H), 4.38 (q, 2H), 1.58 (s, 9H), 1.40 (t, 3H).

Step 2. Preparation of 5-(*tert*-butyl) 3-ethyl 1-isopropyl-7-(trifluoromethyl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C78)** and 2-((3-(ethoxycarbonyl)-2-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)oxy)-2-methylpropan-1-ylium **(C79)**

To a solution of **C77** (408 mg, 1.12 mmol) in EtOH (4.5 mL) was added isopropylhydrazine hydrochloride (CAS: 16726-41-3; 148 mg, 1.34 mmol) and then pyridine

(132 mg, 1.67 mmol). The reaction mixture was stirred at 55 °C for 20 h and then concentrated *in vacuo* to give a yellow-orange residue. The residue was diluted with EtOAc (20 mL) and washed with $NaHCO_3$ (20 mL). The aqueous layer was back-extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and concentrated *in vacuo* to give an orange oil. The oil was dissolved in DCM then preabsorbed on (1:1) silica gel: Celite and purified by column chromatography (silica gel, 0-100% EtOAc: heptane) to provide **C78** (0.315 g, 69.9% yield) as a gum and **C79** (7.70 mg, 1.71% yield) as a light-yellow solid.

C78: (LC/MS) m/z $(M+H)^+$ = 404.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.46 (m, 1H), 5.02 (s, 2H), 4.73 – 4.63 (m, 1H), 4.39 (q, 2H), 1.55 (s, 9H), 1.50 (d, 6H), 1.39 (t, 3H).

C79: (LC/MS) m/z $(M+H)^+$ = 404.5; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.33 (m, 1H), 5.51 – 5.49 (m, 1H), 4.97 (s, 2H), 4.35 (q, 2H), 1.55 (s, 9H), 1.48 (d, 6H), 1.39 (t, 3H).

Step 3. Preparation of *rac*-5-(*tert*-butyl) 3-ethyl (*R*)-1-isopropyl-7-(trifluoromethyl)-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C80)**

To a suspension of Pd/C (CAS: 7440-05-3; 83 mg, 5% wt, 0.039 mmol) in EtOH (0.5 mL) was added a light-yellow solution of **C78** (0.30 g, 0.75 mmol) in EtOH (1.5 mL). The source vial was rinsed with EtOH (0.5 mL x 2), and then the rinses were added to the reaction mixture for a total volume of EtOH (3 mL). The reaction mixture was stirred at room temperature overnight in a Hastelloy reactor at H_2 gas (50 psi). The suspension was filtered through Celite (0.5 g) with a prepacked plastic filter funnel. The filter cake was eluted with EtOH. The grey filtrate was concentrated *in vacuo* to give a grey residue.

The same reaction was set up again. To a reaction mixture of Pd/C (98 mg, 5 wt%, 0.046 mmol) in EtOH (0.5 mL) was added the solution of the crude residue dissolved in EtOH (1.5 mL). The reaction mixture was stirred at room temperature overnight in a Hastelloy reactor at H_2 gas (50 psi). The suspension was filtered through Celite (0.5 g) with a prepacked plastic filter funnel. The filter cake was eluted with EtOH. The grey filtrate was concentrated *in vacuo* to provide a grey solid. The solid was purified by column chromatography (silica gel, 0-50% EtOAc: heptane) to provide **C80** (0.24 g, 78% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 406.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 – 5.23 (m, 1H), 5.13 – 4.76 (m, 2H), 4.59 – 4.47 (m, 1H), 4.44 – 4.34 (m, 3H), 4.29 – 4.08 (m, 2H), 3.60 – 3.44 (m, 1H), 3.08 (dd, 1H), 1.59 – 1.55 (m, 9H), 1.43 – 1.35 (m, 6H).

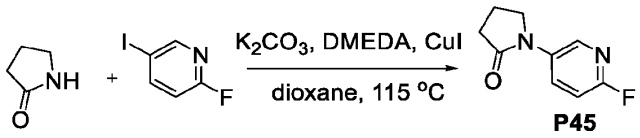
Step 4. Preparation of *rac*-ethyl (*R*)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P44)**

To **C80** (0.234 g, 0.577 mmol) was added 4N HCl in dioxane (1.44 mL) dropwise. The reaction mixture was stirred at 40 °C for 40 min then concentrated under nitrogen gas then dried further under high vacuum to provide **P44** (0.210 g, crude) as a white solid. (LC/MS) m/z

$(M+H)^+$ = 306.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.41 (br s, 1H), 8.55 (br s, 1H), 4.91 – 4.80 (m, 1H), 4.76 – 4.65 (m, 1H), 4.40 – 4.20 (m, 3H), 3.92 (d, 1H), 3.74 – 3.64 (m, 1H), 3.55 – 3.45 (m, 1H), 1.44 (d, 3H), 1.36 (d, 3H), 1.30 (t, 3H).

Preparation 45

1-(6-Fluoropyridin-3-yl)pyrrolidin-2-one **(P45)**



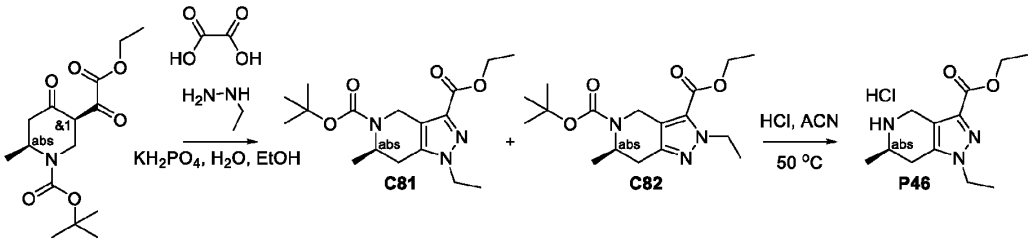
P45

Step 1. Preparation of 1-(6-fluoropyridin-3-yl)pyrrolidin-2-one **(P45)**

A reaction mixture of 2-fluoro-5-iodopyridine (CAS: 171197-80-1; 2.00 g, 8.97 mmol), pyrrolidin-2-one (CAS: 616-45-5; 0.763 g, 8.97 mmol), K_2CO_3 (3.72 g, 26.9 mmol), DMEDA (0.158 g, 1.79 mmol) and CuI (0.342 g, 1.79 mmol) in dioxane (40 mL) was heated to 115 °C for 16 h under nitrogen gas. The suspension was filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-60% EtOAc: PE) to provide **P45** (1.40 g, 86.6% yield) as a light-yellow solid. (LC/MS) m/z $(M+H)^+$ = 181.0; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 – 8.43 (m, 1H), 8.36 – 8.29 (m, 1H), 7.22 (dd, 1H), 3.89 – 3.83 (m, 2H), 2.54 – 2.51 (m, 1H), 2.50 – 2.48 (m, 1H), 2.14 – 2.04 (m, 2H).

Preparation 46

Ethyl (*R*)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P46)**



C81 **C82** **P46**

Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl (*R*)-1-ethyl-6-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C81)** and 5-(*tert*-butyl) 3-ethyl (*R*)-2-ethyl-6-methyl-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C82)**

A reaction mixture of H_2O (8.8 mL), EtOH (8.8 mL), *tert*-butyl (2*S*,5*RS*)-5-(2-ethoxy-2-oxoacetyl)-2-methyl-4-oxopiperidine-1-carboxylate (CAS: 2171296-27-6; 1.65 g, 5.27 mmol), ethylhydrazine oxalate (0.949 g, 6.32 mmol) and KH_2PO_4 (1.00 g, 7.37 mmol) was stirred at room temperature for 2 h. The yellow slurry was checked by LCMS, which showed **C81** (LC/MS) m/z $(M+H)^+$ = 338.3 at 1.69 min retention time and **C82** (LC/MS) m/z $(M+H)^+$ = 338.3 at 1.94 min retention time. The reaction mixture was diluted with H_2O and extracted with DCM (3x). The combined organic layer was dried with Na_2SO_4 and then purified by column

chromatography (silica gel, 0-100% EtOAc: heptane) to provide **C81** (1.53 g, 86.0% yield) and **C82** (30.0 mg, 1.70% yield).

C81: ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 4.88 (d, 1H), 4.78 – 4.65 (m, 1H), 4.33 – 4.17 (m, 2H), 4.14 – 3.94 (m, 3H), 2.85 (dd, 1H), 2.68 – 2.60 (m, 1H), 1.42 (s, 9H), 1.33 – 1.26 (m, 6H), 1.03 (d, 3H).

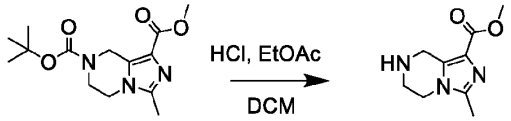
C82: ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 4.91 (d, 1H), 4.78 – 4.63 (m, 1H), 4.54 – 4.36 (m, 2H), 4.35 – 4.15 (m, 2H), 4.09 – 3.96 (m, 2H), 3.38 – 3.26 (m, 1H), 2.82 – 2.65 (m, 2H), 2.56 – 2.51 (m, 1H), 2.47 - 2.36 (m, 1H), 2.28 – 2.12 (m, 2H), 1.35 – 1.27 (m, 6H), 1.10 – 1.06 (m, 3H), 1.04 – 0.99 (m, 3H).

Step 2. Preparation of ethyl (*R*)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(P46)**

To a solution of **C81** (1.00 g, 2.96 mmol) in ACN (10 mL) was added 12.1M HCl (0.216 g, 5.93 mmol). The reaction mixture was stirred at 50 °C for 25 h and 15 min, then concentrated *in vacuo*. The residue was diluted with ACN and then concentrated *in vacuo*. The residue was diluted with DCM and concentrated *in vacuo* (2x) to provide **P46** (0.730 g, crude) as a yellow foam. The yellow foam was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 238.2. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 9.33 – 9.24 (m, 1H), 9.07 – 8.93 (m, 1H), 4.38 – 4.10 (m, 6H), 3.48 – 3.39 (m, 1H), 3.16 (dd, 1H), 2.71 (dd, 1H), 1.41 – 1.37 (m, 3H), 1.31 (dt, 6H).

Preparation 47

Methyl 3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate **(47)**



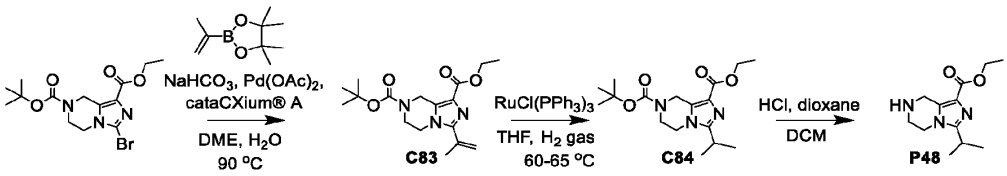
P47

Step 1. Preparation of methyl 3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(P47)**

To a solution of 7-(*tert*-butyl) 1-methyl 3-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (CAS: 1359655-89-2, 0.190 g, 0.643 mmol) in DCM (5.0 mL) was added 2M HCl in EtOAc (5.0 mL) at 10 °C. The reaction mixture was stirred at room temperature for 16 h. The reaction mixture became a white suspension concentrated *in vacuo* to provide the **P47** (0.149 g, crude) as a white solid. This was used in the next step without further purification. ^{1}H NMR (400 MHz, CD_3OD) δ 4.80 (s, 2H), 4.51 (t, 2H), 4.00 (s, 3H), 3.84 (t, 2H), 2.71 (s, 3H).

Preparation 48

Ethyl 3-isopropyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(P48)**



Step 1. Preparation of 7-(*tert*-butyl) 1-ethyl 3-(prop-1-en-2-yl)-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C83)**

A solution of 7-(*tert*-butyl) 1-ethyl 3-bromo-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (CAS: 2108354-93-2; 1.00 g, 2.67 mmol), 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (CAS: 126726-62-3, 0.808 g, 4.81 mmol), $NaHCO_3$ (0.673 g, 8.02 mmol), cataCXium® A (0.192 g, 0.534 mmol) and $Pd(OAc)_2$ (60.0 mg, 0.267 mmol) in (4:1) DME: H_2O (16 mL: 4 mL) was degassed with nitrogen gas for 5 min. The reaction solution was stirred at 90 °C for 16 h and then concentrated *in vacuo*. The residue was dissolved in DCM (50 mL) and then extracted with EtOAc (3 x 50 mL). The combined organic layer was dried with Na_2SO_4, filtered, and then concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (silica gel, 0-20% EtOAc: PE) to provide **C83** (0.856 g, 95.5% yield) as a light-yellow solid. (LC/MS) m/z $(M+H)^+$ = 336.2.

Step 2. Preparation of 7-(*tert*-butyl) 1-ethyl 3-isopropyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C84)**

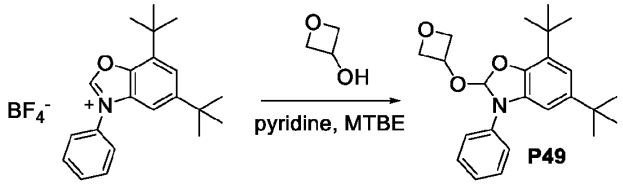
To the suspension of **C83** (0.86 g, 2.5 mmol) in THF (20 mL) was added $RuCl(PPh_3)_3$ (0.24 g, 0.25 mmol). The reaction mixture was degassed with hydrogen gas and then stirred under a hydrogen atmosphere (50 psi) from 60-65 °C for 48 h. The suspension was concentrated *in vacuo, and* then the residue was purified by column chromatography (silica gel, 0-20% THF: PE) to provide **C84** (0.67 g, 77% yield) as a brown solid. (LC/MS) m/z $(M+H)^+$ = 338.3. ^1H NMR (400 MHz, $CDCl_3$) δ 4.87 (s, 2H), 4.36 (q, 2H), 3.92 (t, 2H), 3.82 (t, 2H), 3.03 – 2.89 (m, 1H), 1.50 (s, 9H), 1.43 – 1.32 (m, 9H).

Step 3. Preparation of ethyl 3-isopropyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(P48)**

To a solution of **C84** (0.67 g, 2.0 mmol) in DCM (10 mL) was added 2M HCl in dioxane (20 mL). The reaction solution was stirred at room temperature for 2 h then was concentrated *in vacuo* and was dried further by high *vacuo* to provide **P48** (0.54 g, crude) as a solid. The solid was used directly in the next step without further purification.

Preparation 49

5,7-Di-*tert*-butyl-2-(oxetan-3-yloxy)-3-phenyl-2,3-dihydrobenzo[*d*]oxazole **(P49)**

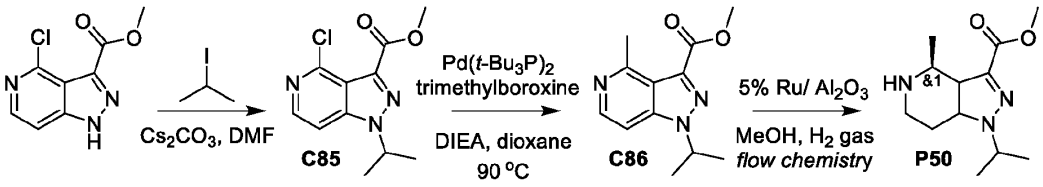


Step 1. Preparation of 5,7-di-*tert*-butyl-2-(oxetan-3-yloxy)-3-phenyl-2,3-dihydrobenzo[*d*]oxazole **(P49)**

A reaction mixture of 3-hydroxyoxetane (CAS: 7748-36-9; 41 mg, 0.55 mmol) and deoxazole (CAS: 1207294-92-5; 0.22 g, 0.55 mmol) in MTBE (3 mL) was degassed with nitrogen gas (2x). The suspension was stirred at room temperature for 5 min before adding pyridine (43 mg, 0.55 mmol). The reaction mixture was stirred for 30 min to provide a solution of **P49** (0.21 g, crude). The solution was used directly in the next step without further purification.

Preparation 50

rac-Methyl (4*R*)-1-isopropyl-4-methyl-3*a*,4,5,6,7,7*a*-hexahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P50)**



Step 1. Preparation of methyl 4-chloro-1-isopropyl-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C85)**

To a solution of methyl 4-chloro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (CAS: 1658466-48-8; 6.00 g, 28.3 mmol) in DMF (120 mL) was added Cs_2CO_3 (18.5 g, 56.7 mmol) and 2-iodopropane (CAS: 75-30-9; 7.23 g, 42.5 mmol). The reaction mixture was stirred at room temperature for 3 h, diluted with EtOAc (100 mL), and washed with brine (3 x 300 mL). The organic layer was dried with Na_2SO_4 and then concentrated *in vacuo*. The yellow oil was purified by column chromatography (silica gel, 0-37% EtOAc: hexane) to provide **C85** (3.30 g, 45.9% yield). (LC/MS) m/z $(M+H)^+$ = 254.0. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.26 (d, 1H), 7.93 (d, 1H), 5.22 – 5.07 (m, 1H), 3.93 (s, 3H), 1.49 (d, 6H).

Step 2. Preparation of methyl 1-isopropyl-4-methyl-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C86)**

To a solution of **C85** (2.10 g, 8.28 mmol), trimethylboroxine (CAS: 823-96-1; 8.31 g, 33.1 mmol) in dioxane (60 mL) was added DIEA (4.28 g, 33.1 mmol) and Pd(*t*-$Bu_3P)_2$ (0.635 g, 1.24 mmol). The reaction mixture was degassed with nitrogen gas and then stirred at 90 °C for 12 h.

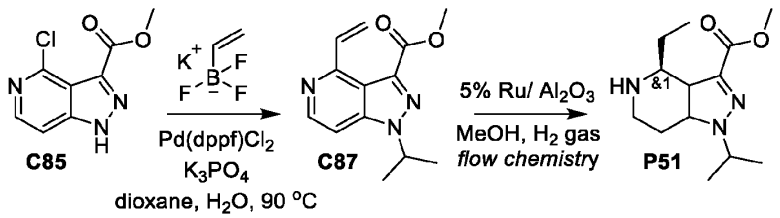
The suspension was diluted with EtOAc (100 mL), washed with brine (2 x 150 mL), dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-50% EtOAc: hexane) to provide **C86** (2.10 g, crude) as an orange gum. The gum was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 234.0. ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, 1H), 7.24 (d, 1H), 4.96 – 4.83 (m, 1H), 4.03 (s, 3H), 3.06 (s, 3H), 1.65 – 1.61 (m, 6H).

Step 3. Preparation of *rac*-methyl (4*R*)-1-isopropyl-4-methyl-3*a*,4,5,6,7,7*a*-hexahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P50)**

The reaction was carried out via flow chemistry. **C86** (1.80 g, 7.72 mmol) was dissolved in MeOH (40 mL). The solution was pumped with a flow rate of 0.3 mL/min, and the H_2 had a 30 mL/ min rate. The solution passed through the fixed bed (1/4" mm) packed with granular catalyst 5% Ru/Al_2O_3 with a 5.0 mL volume and was hydrogenated at 60 °C via flow at 2.0 MPa H_2. The reaction mixture was collected from the reactor output to provide **P50** (1.85 g, crude) as a black oil. The oil was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 238.2. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 4.61 – 4.42 (m, 2H), 4.24 – 4.01 (m, 1H), 3.86 – 3.75 (m, 3H), 3.04 – 2.77 (m, 4H), 1.49 (d, 3H), 1.38 (dd, 6H).

Preparation 51

rac-Methyl (4*R*)-4-ethyl-1-isopropyl-3*a*,4,5,6,7,7*a*-hexahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P51)**



Step 1. Preparation of methyl 1-isopropyl-4-vinyl-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C87)**

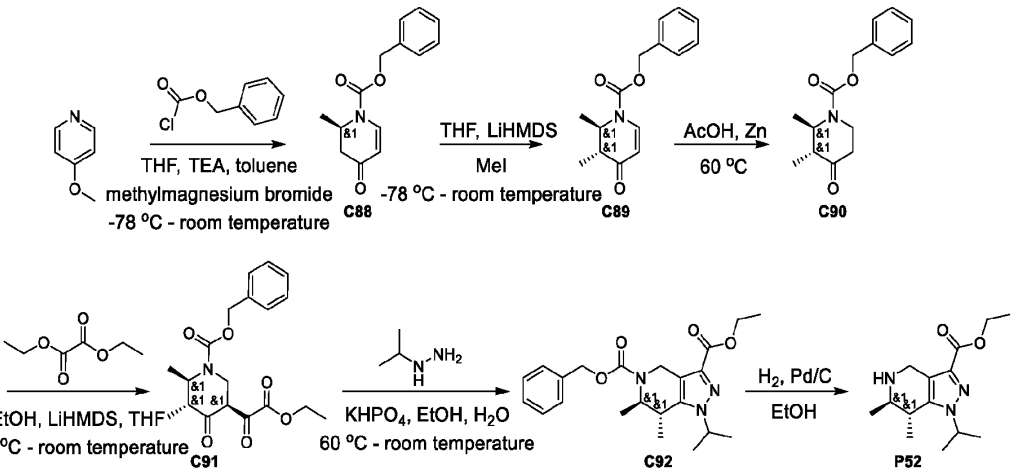
To a reaction mixture of **C85** (1.00 g, 3.94 mmol), potassium vinyltrifluoroborate (CAS: 13682-77-4; 0.792 g, 5.91 mmol) and K_3PO_4 (2.09 g, 9.85 mmol) in dioxane (10.0 mL) and H_2O (3.5 mL) was added $Pd(dppf)Cl_2$ (0.288 g, 0.394 mmol). The suspension was degassed with nitrogen gas for 3 min and then stirred at 90 °C for 2 h. The reaction mixture was filtered, and then the filter cake was washed with EtOAc (50 mL). The filtrate was concentrated *in vacuo*. The yellow gum was purified by column chromatography (silica gel, 0-40% EtOAc: hexane) to provide **C87** (0.700 g, 72.4% yield) as a light yellow solid. (LC/MS) m/z $(M+H)^+$ = 246.1. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.45 (d, 1H), 8.07 (dd, 1H), 7.79 (d, 1H), 6.51 (dd, 1H), 5.59 (dd, 1H), 5.19 – 5.08 (m, 1H), 3.93 (s, 3H), 1.50 (d, 6H).

Step 2. Preparation of *rac*-methyl (4*R*)-4-ethyl-1-isopropyl-3*a*,4,5,6,7,7*a*-hexahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P51)**

The reaction was carried out via flow chemistry. **C87** (0.300 g, 1.22 mmol) was dissolved in MeOH (20 mL). The solution was pumped with a flow rate of 0.3 mL/min, and the H_2 had a 30 mL/ min rate. The solution passed through the fixed bed (1/4" mm) packed with granular catalyst 5% Ru/Al_2O_3 with a 5.0 mL volume and was hydrogenated at 60 °C via flow at 2.0 MPa H_2. The reaction mixture was collected from the reactor output to provide **P51** (0.280 g, crude) as a brown oil. The oil was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 252.0. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 9.75 (s, 1H), 9.23 (s, 1H), 4.59 – 4.50 (m, 1H), 3.78 (s, 3H), 3.07 – 2.89 (m, 2H), 2.45 – 2.41 (m, 2H), 2.00 – 1.75 (m, 2H), 1.35 (dd, 6H), 1.02 (t, 3H).

Preparation 52

rac-Ethyl (6*R*,7*R*)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P52)**



Step 1. Preparation of *rac*-benzyl (*R*)-2-methyl-4-oxo-3,4-dihydropyridine-1(2*H*)-carboxylate **(C88)**

To a round bottom flask was added 4-methoxypyridine (CAS: 620-08-6; 32.6 mL), THF (641.4 mL), and TEA (4.5 mL) sequentially. The solution was cooled to -78 °C, and then 3M benzyl chloroformate in toluene (109.0 mL) was added dropwise to give a white slurry. 3.4M methylmagnesium bromide solution (55.6 mL) dropwise was added to the suspension. The reaction mixture was stirred at -78 °C and slowly warmed to room temperature over 24 h. The reaction mixture was cooled to 0 °C and quenched via a portion-wise addition of 1M aqueous HCl. The aqueous mixture was extracted with DCM (3x). The organic layer was combined, then dried with Na_2SO_4 and purified by column chromatography (silica gel, 0-50% EtOAc: heptane) to provide **C88** (51.5 g, 65.5% yield) as a clear oil. (LC/MS) m/z $(M+H)^+$ = 246.4. ^1H NMR (400

MHz, $(CD_3)_2SO$) δ 7.78 (dd, 1H), 7.48 – 7.28 (m, 5H), 5.33 – 5.21 (m, 3H), 4.68 – 4.56 (m, 1H), 2.89 (dd, 1H), 2.24 – 2.14 (m, 1H), 1.15 (d, 3H).

Step 2. Preparation of *rac*-benzyl (2*R*,3*R*)-2,3-dimethyl-4-oxo-3,4-dihydropyridine-1(2*H*)-carboxylate **(C89)**

A reaction mixture of **C88** (10.0 g, 40.8 mmol) in THF (102 mL) was cooled to -78 °C, then 1M LiHMDS in THF (42.8 mL) was added dropwise and stirred at -78 °C for 10 min. After stirring for a few min, MeI (3.1 mL) was added dropwise at -78 °C to the reaction mixture and then warmed to room temperature over 30 min. The suspension was stirred at room temperature for 9 h and then quenched with brine. The pH of the aqueous layer was adjusted to pH = 1 using 12M aqueous HCl. The reaction mixture was extracted with EtOAc (2x), and the organic layers were combined and then dried with Na_2SO_4. The mixture was purified by column chromatography (silica gel, 0-40% MTBE: heptane) to provide **C89** (7.80 g, 73.6% yield) as a yellow oil. ^{1}H NMR (400 MHz, CD_3OD) δ 7.84 (dd, 1H), 7.47 – 7.32 (m, 5H), 5.36 – 5.20 (m, 3H), 4.40 (q, 1H), 2.27 (q, 1H), 1.21 (d, 3H), 1.15 (d, 3H).

Step 3. Preparation of *rac*-benzyl (2*R*,3*R*)-2,3-dimethyl-4-oxopiperidine-1-carboxylate **(C90)**

To a round bottom flask was added **C89** (12.8 g, 49.4 mmol), AcOH (82.3 mL), and Zn (12.9 g, 197 mmol) sequentially, then stirred at 60 °C for 5 h. The reaction mixture was concentrated *in vacuo,* then saturated $NaHCO_3$ and extracted with DCM (3x). The combined organic layer was purified by column chromatography (silica gel, 0-50% EtOAc: heptane) to provide **C90** (10.1 g, 78.3% yield) as a clear oil. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.44 – 7.28 (m, 5H), 5.17 – 5.06 (m, 2H), 4.13 (dd, 1H), 4.07 – 3.96 (m, 1H), 3.53 – 3.41 (m, 1H), 2.57 – 2.44 (m, 2H), 2.33 – 2.23 (m, 1H), 1.21 (d, 3H), 1.05 (d, 3H).

Step 4. Preparation of *rac*-benzyl (2*R*,3*R*,5*R*)-5-(2-ethoxy-2-oxoacetyl)-2,3-dimethyl-4-oxopiperidine-1-carboxylate **(C91)**

A reaction mixture of **C90** (0.430 g, 1.65 mmol), EtOH (3.29 mL), and diethyl oxalate (0.24 mL) was cooled to -78 °C, then 1M LiHMDS in THF (1.89 mL) was added. The suspension was stirred at room temperature for 17 h and then quenched with a mixture of 1M aqueous HCl, brine, and DCM. The aqueous layer was extracted with (2:1, MTBE: DCM, 2x). The organic layers were combined and then dried with Na_2SO_4 and concentrated *in vacuo* to provide **C91** (0.590 g, crude) as a yellow oil. The oil was used directly in the next step without further purification.

Step 5. Preparation of *rac*-5-benzyl 3-ethyl (6*R*,7*R*)-1-isopropyl-6,7-dimethyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate **(C92)**

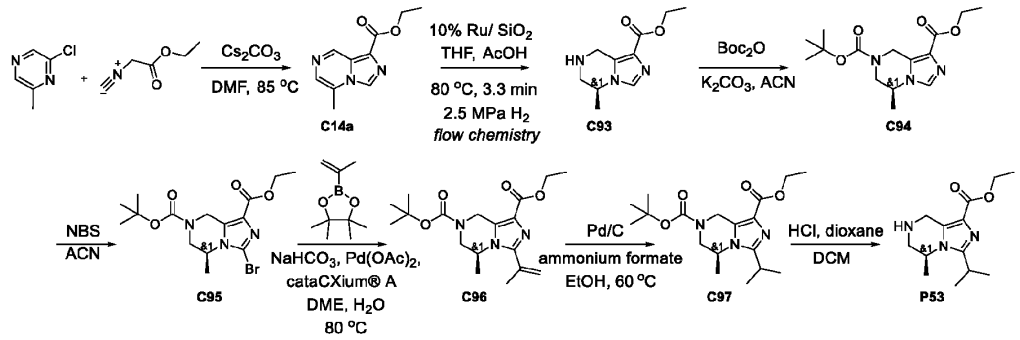
A reaction mixture of **C91** (0.590 g, 1.63 mmol), $KHPO_4$ (0.311 g, 2.29 mmol) and isopropylhydrazine HCl (217 mg, 1.96 mmol) in EtOH (2.7 mL) and H_2O (2.7 mL) was stirred at 60 °C for 2.5 h then stirred at room temperature for 24 h. The suspension was diluted with H_2O and then extracted with DCM (3x). The organic layers were combined and then purified with column chromatography (silica gel, 0-60% EtOAc: heptane) to provide **C92** (0.322 g, 49.4% yield) as a clear oil.

Step 6. Preparation of *rac*-ethyl (6*R*,7*R*)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(P52)**

In a reactor was added Pd/C (10 wt%, 0.213 g, 2.00 mmol) in EtOH (1 mL), then added solution of **C92** (0.800 g, 2.00 mmol) in EtOH (5 mL). The suspension was degassed with hydrogen gas and then stirred under a hydrogen atmosphere (120 psi) at room temperature for 1 h. The reaction mixture was filtered through Celite and then washed with *tert*-amyl alcohol. The filtrate was concentrated *in vacuo* to provide **P52** (0.531 g, crude) as a yellow oil. The oil was used directly in the next step without further purification. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 4.57 – 4.46 (m, 1H), 4.23 (q, 2H), 3.82 – 3.68 (m, 2H), 2.84 – 2.74 (m, 1H), 2.62 – 2.55 (m, 1H), 1.43 (d, 3H), 1.39 – 1.31 (m, 6H), 1.22 – 1.18 (m, 3H), 1.05 – 1.01 (m, 3H).

Preparation 53

rac-Ethyl (*R*)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(P53)**



Step 1. Preparation of ethyl 5-methylimidazo[1,5-a]pyrazine-1-carboxylate **(C14a)**

To a mixture of 2-chloro-6-methylpyrazine (CAS: 38557-71-0, 10.0 g, 77.8 mmol) in DMF (150.0 mL) was added Cs_2CO_3 (38.0 g, 117 mmol) and ethyl 2-isocyanoacetate (CAS: 2999-46-4, 17.8 g, 156 mmol) at 15 °C. The reaction was heated to 85 °C for 16 h, then diluted with EtOAc (300 mL). The light brown reaction mixture was filtered, and the filtrate was concentrated *in vacuo*. The brown residue was diluted with (1:1, EtOAc: THF) and filtered. The filter cake was dissolved in (1:1, H_2O: EtOAc) and then extracted with EtOAc (150 mL). The combined organic phase was dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-100% EtOAC: PE) to provide **C14a** (7.71 g,

48.3% yield) as a light-brown solid. (LC/MS) m/z $(M+H)^+$ = 206.1. ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.16 (s, 1H), 7.66 (s, 1H), 4.52 (q, 2H), 2.65 (s, 3H), 1.48 (t, 3H).

Step 2. Preparation of *rac*-ethyl (*R*)-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate acetate **(C93)**

The reaction was carried out via flow chemistry. **C14a** (7.71 g, 37.6 mmol) was dissolved in THF (155 mL) and AcOH (40 mL) and then was pumped with a flow rate of 0.3 mL/min, and the H_2 had a rate of 30 mL/ min. The solution passed through the fixed bed ((1/4") mm) packed with granular catalyst 10% Ru/SiO_2 (2.80 g, 2.76 mmol) with a 5.0 mL volume and was hydrogenated for 3.3 min at 80 °C via flow at 2.5 MPa H_2. The flow rate of H_2 was 100 mL/ min. The reaction mixture was collected after 10 min and then concentrated *in vacuo* to remove THF. The suspension was stirred for 1-2 h and then filtered. The filtrate was concentrated *in vacuo* to provide **C93** (5.50 g, crude) as a light-brown oil. The oil was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 210.1.

Step 3. Preparation of *rac*-7-(*tert*-butyl) 1-ethyl (*R*)-5-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C94)**

To a solution of **C93** (7.50 g, 19.3 mmol) in ACN (100 mL) was added Boc_2O (6.31 g, 28.9 mmol) and K_2CO_3 (10.7 g, 77.1 mmol) at room temperature. The reaction was stirred at room temperature for 16 h and then diluted with EtOAc (100 mL). The suspension was filtered then the filtrate was concentrated *in vacuo.* The residue was purified by column chromatography (silica gel; 0-100% EtOAc: PE) to provide **C94** (5.30 g, 93.1% yield) as an off-white solid. (LC/MS) m/z $(M+H)^+$ = 310.2. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 4.96 – 4.78 (m, 2H), 4.41 – 4.22 (m, 3H), 3.95 – 3.90 (m, 1H), 3.48 – 3.43 (m, 1H), 1.55 – 1.49 (m, 12H), 1.39 (t, 3H).

Step 4. Preparation of *rac*-7-(*tert*-butyl) 1-ethyl (*R*)-3-bromo-5-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C95)**

To a solution of **C94** (3.20 g, 10.8 mmol) in ACN (30.0 mL) was added a solution of NBS (2.89 g, 16.3 mmol) in ACN (20.0mL). The reaction mixture was stirred at room temperature for 16 h and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-40% EtOAc: PE) to provide **C95** (2.57 g, 64.0% yield) as a white solid. (LC/MS) m/z $(M+2H)^+$ = 390.0. ^1H NMR (400 MHz, $CDCl_3$) δ 5.59 – 5.25 (m, 1H), 4.51 – 4.25 (m, 5H), 3.40 – 3.12 (m, 1H), 1.51 (s, 9H), 1.45 – 1.29 (m, 6H).

Step 5. Preparation of *rac*-7-(*tert*-butyl) 1-ethyl (*R*)-3-isopropyl-5-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C96)**

A solution of **C95** (1.00 g, 2.58 mmol), 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (CAS: 126726-62-3, 0.779 g, 4.64 mmol), $NaHCO_3$ (0.649 g, 7.73 mmol),

cataCXium® A (0.185 g, 0.515 mmol) and $Pd(OAc)_2$ (57.8 mg, 0.258 mmol) in (4:1) DME: H_2O (16 mL: 4 mL) was degassed with nitrogen gas for 5 min. The reaction solution was stirred at 80 °C for 15 h, then filtered and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-35% EtOAc: PE) to provide **C96** (0.810 g, 90.0% yield) as a gum. (LC/MS) m/z $(M+H)^+$ = 350.2. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 5.49 – 5.38 (m, 2H), 5.26 – 5.05 (m, 1H), 4.79 – 4.65 (m, 1H), 4.58 – 4.36 (m, 1H), 4.33 – 3.97 (m, 4H), 2.10 – 2.06 (m, 3H), 1.43 (s, 9H), 1.31 – 1.24 (m, 3H), 1.23 – 1.16 (m, 3H).

Step 6. Preparation of *rac*-7-(*tert*-butyl) 1-ethyl (*R*)-5-methyl-3-(prop-1-en-2-yl)-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate **(C97)**

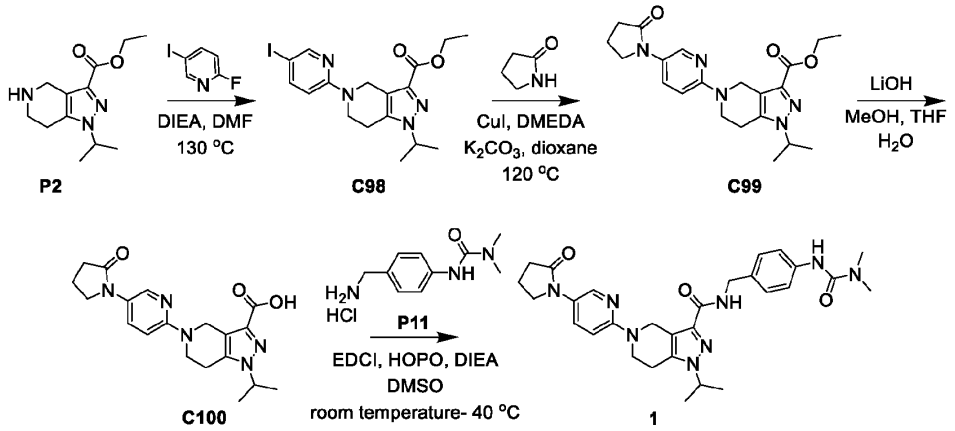
To a solution of **C96** (0.810 g, 2.32 mmol) in EtOH were added ammonium formate (2.19 g, 34.8 mmol) and Pd/C (0.370 g, 0.348 mmol). The reaction mixture was stirred at 60 °C under argon gas for 1 h and then filtered through celite. The filter cake was washed with EtOH (3 x 30 mL). The filtrate was concentrated *in vacuo* and then dissolved in DCM (50 mL). The solution was washed with brine (3 x 50 mL). The organic layer was concentrated *in vacuo* to provide **C97** (0.715 g, crude). The crude was used directly into the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 352.2.

Step 7. Preparation of *rac*-ethyl (*R*)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(P53)**

To a solution of **C97** (0.715 g, 2.03 mmol) in DCM (10 mL) was added 2M HCl in dioxane (20 mL). The reaction mixture was stirred for 2 h at room temperature, then concentrated *in vacuo* and lyophilized to provide **P53** (0.710 g, crude) as a gum. The gum was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 252.2.

Example 1

N-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(1)**



Step 1. Preparation of ethyl 5-(5-iodopyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C98**)

A mixture of **P2** (1.36 g, 4.98 mmol), 2-fluoro-5-iodopyridine (CAS: 171197-80-1, 1.22 g, 5.48 mmol), and DIEA (1.93 g, 14.9 mmol) in DMF (25.0 mL) was stirred at 130 °C for 16 h. The brown reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica gel, 0- 20% EtOAc: PE) to provide **C98** (0.61 g, 27.8%) as a white solid. (LC/MS) m/z $(M+H)^+$ = 441.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32- 8.31 (m, 1H), 7.68 (dd, 1H), 6.58 (d, 1H), 4.60 (s, 2H), 4.52- 4.38 (m, 3H), 4.03 (t, 2H), 2.80 (t, 2H), 1.52 (d, 6H), 1.44-1.40 (m, 3H).

Step 2. Preparation of ethyl 1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C99**)

A mixture of **C98** (0.400 g, 0.909 mmol), pyrrolidine-2-one (0.116 g, 1.36 mmol), CuI (34.6 mg, 0.182 mmol), DMEDA (16.0 mg, 0.182 mmol) and K_2CO_3 (0.377 g, 2.73 mmol) in dioxane (10.0 mL) was heated at 120 °C for 16 h under nitrogen. The reaction was concentrated *in vacuo,* and then the residue was purified by column chromatography (silica gel, 0-30% THF:PE) to provide **C99** (0.36 g, 99.7% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 398.2.

Step 3. Preparation of 1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C100**)

To a solution of **C99** (0.360 g, 0.906 mmol) in THF (5.00 mL), MeOH (1.25 mL) and H_2O (2.50 mL) was added LiOH (57.5 mg, 2.40 mmol) then stirred at room temperature for 1 h and 30 min. The solution was concentrated *in vacuo and* then acidified to pH=5-6 with 2N HCl. An off-white solid precipitated was filtered, then washed with H_2O (3 x 50 mL), dried, then lyophilized to provide **C100** (0.27 g, 80.7%) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) δ 8.29 (d, 1H), 7.82 (dd, 1H), 6.91 (d, 1H), 4.67 (s, 2H), 4.60- 6.45 (m, 1H), 3.96 (t, 2H), 3.88- 3.83 (m, 2H), 2.86 (t, 2H), 2.60- 2.52 (m, 2H), 2.24 – 2.13 (m, 2H), 1.47 (d, 6H).

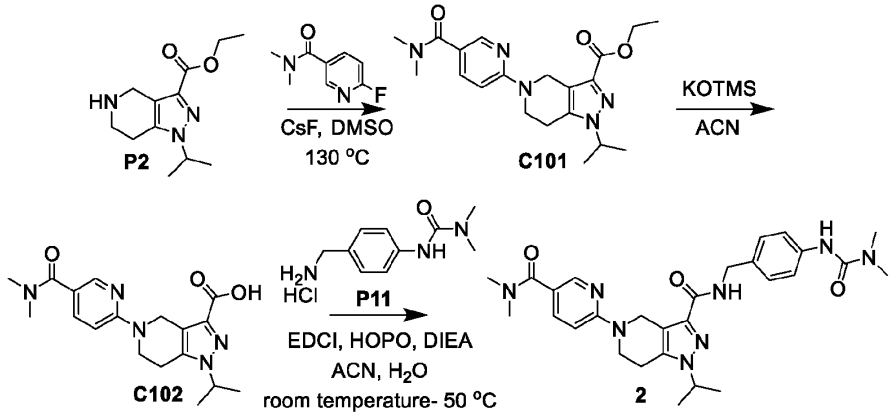
Step 4. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**1**)

A solution of **C100** (80.0 mg, 0.217 mmol), HOPO (71.0 mg, 0.639 mmol), EDCI (99.6 mg, 0.520 mmol) and DIEA (0.140 g, 1.08 mmol) in DMSO (2.0 mL) were stirred at room temperature for 10 min. to the reaction mixture was added **P11** (74.6 mg, 0.325 mmol) then heated to 40 °C and stirred for 2 h. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 μm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (NH_4OH-NH_4HCO_3), 18 to 58% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **1** (72.2 mg, 61.2% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 545.4. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33- 8.27 (m, 2H), 8.23 (s, 1H), 7.89 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.20- 7.15 (m, 2H), 6.90 (d, 1H), 4.65 (s, 2H), 4.53- 4.42 (m, 1H), 4.35 (d,

2H), 3.87 (t, 2H), 3.76 (t, 2H), 2.91 (s, 6H), 2.80 (t, 2H), 2.43 (t, 2H), 2.10- 2.00 (m, 2H), 1.39 (d, 6H).

Example 2

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**2**)



Step 1. Preparation of ethyl 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C101**)

To a mixture of **P2** (70.0 g, 256 mmol) and CsF (97.1 g, 639 mmol) in DMSO (0.7 L) was added 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3, 57.3 g, 256 mmol). The reaction was stirred at 130 °C for 8 h. The reaction was diluted with H_2O (6 L) and then extracted with MeOH: DCM (1:10, 3 x 2 L). The combined organic layer was washed with brine (2 x 3 L), dried with Na_2SO_4, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE) to provide **C101** (72.0 g, 73.1% yield) as a pale yellow solid. (LC/MS) m/z $(M+H)^+$ = 386.2. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.25 (d, 1H), 7.65 (dd, 1H), 6.91 (d, 1H), 4.74 (s, 2H), 4.58-4.47 (m, 1H), 4.30 (q, 2H), 3.96 (t, 2H), 2.97 (s, 6H), 2.83 (t, 2H), 1.38 (d, 6H), 1.32 (t, 3H).

Step 2. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C102**)

The reaction was conducted in two batches then combined for purification. At room temperature under nitrogen, a mixture of **C101** (42.0 g, 109 mmol) in ACN (420 mL) was added KOTMS (28.0 g, 218 mmol) then stirred at room temperature for 1 h to afford the first batch. The first batch was acidified with 2M HCl in dioxane (109 mL, 7.95 g, 218 mmol) to pH= 5-6 then concentrated *in vacuo.*

The first batch's residue was combined with the second batch of the same reaction utilizing **C101** (43.0 g, 112 mmol). The combined reaction mixture was diluted with brine (500 mL) and extracted with MeOH: DCM (1:10, 3 x 1 L). The combined organic layers were dried with Na_2SO_4, filtered, and then concentrated *in vacuo* to provide **C102** (66.0 g, 83.7% yield) as

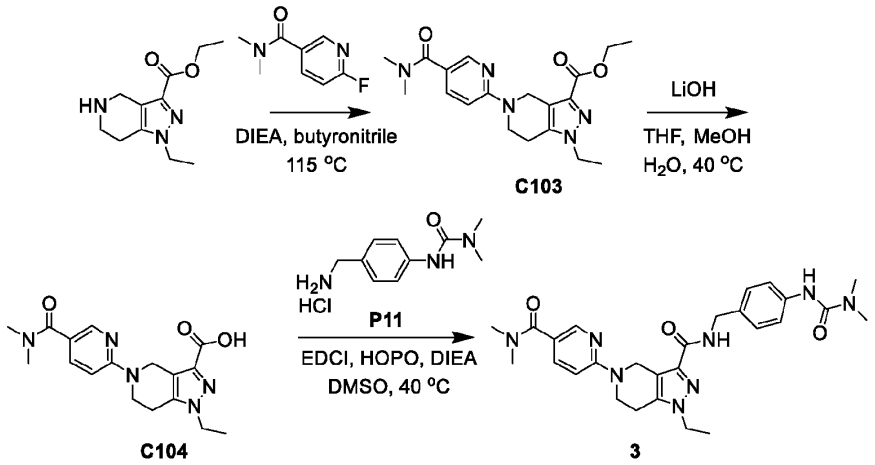
a white solid. This was used in the next step without further purification. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.24 (d, 1H), 7.63 (dd, 1H), 6.92 (d, 1H), 4.70 (s, 2H), 4.54 – 4.37 (m, 1H), 3.94 (t, 2H), 2.97 (s, 6H), 2.79 (t, 2H), 1.37 (t, 6H).

Step 3. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(2)**

To **C102** (70 mg, 0.20 mmol) dissolved in ACN (1.0 mL) and H_2O (0.1 mL) was added HOPO (26 mg, 0.24 mmol) and EDCI (60 mg, 0.31 mmol). The reaction was stirred for 20 min at 50 °C and then cooled to room temperature before DIEA (76 mg, 0.59 mmol) and **P11** (54 mg, 0.24 mmol) were added to the reaction. The mixture was stirred at room temperature for 1 h and 20 min. The reaction was concentrated *in vacuo*, dissolved in DMSO, and acidified by TFA. The acidic residue was purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 15 to 95% of Mobile Phase B over 9.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide **2** (30 mg, 25% yield). (LC/MS) m/z $(M+H)^+$ = 533.4. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ = 8.27 (t, 1H), 8.18 – 8.12 (m, 2H), 7.58 (dd, 1H), 7.34 – 7.30 (m, 2H), 7.11 (d, 2H), 6.84 (d, 1H), 4.68 (s, 2H), 4.45- 4.38 (m, 1H), 4.28 (d, 2H), 3.89 (t, 2H), 2.93-2.88 (m, 6H), 2.84 (s, 6H), 2.76 (t, 2H), 1.33 (d, 6H).

Example 3

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(3)**



Step 1. Preparation of ethyl 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C103**)

To a mixture of ethyl 1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (prepared using similar methods to Preparation 1, 0.350 g, 1.35 mmol) in butyronitrile (5.0 mL) and DIEA (0.697 g, 5.39 mmol) was added 6-fluoro-*N,N*-

dimethylnicotinamide (CAS: 1032251-82-3, 0.249 g, 1.48 mmol) and reaction heated at 115 °C for 17 h. The solution was concentrated *in vacuo*, then redissolved in DCM, and purified by column chromatography (silica gel, 0-5% MeOH: DCM) to provide **C103** (0.209 g, 41.7% yield) as a yellow oil. (LC/MS) m/z $(M+H)^+$ = 372.4. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.23 (d, 1H), 7.64 (dd, 1H), 6.91 (d, 1H), 4.73 (s, 2H), 4.28 (q, 2H), 4.09 (q, 2H), 3.95 (t, 2H), 2.96 (s, 6H), 2.81 (t, 2H), 1.34-1.28 (m, 6H).

Step 2. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C104**)

To **C103** (0.250 g, 0.673 mmol) in THF (2.0 mL), H_2O (2.0 mL), MeOH (0.2 mL) was added LiOH (80.6 mg, 3.37 mmol) at 15 °C. The reaction was heated to 40 °C and stirred for 1 h. The reaction was concentrated *in vacuo* to remove the organic layer, and the aqueous layer was acidified to pH= 3 by 2N HCl. The acidic aqueous phase was concentrated *in vacuo* then purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 0 to 32% of Mobile Phase B over 9 min, 100% then Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **C104** (0.150 g, 64.9% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 344.3. ^{1}H NMR (400 MHz, CD_3OD) δ 8.31 – 8.25 (m, 1H), 7.68 (dd, 1H), 6.91 (d, 1H), 4.77 (s, 2H), 4.15 (q, 2H), 4.06 (t, 2H), 3.09 (s, 6H), 2.86 (t, 2H), 1.40 (t, 3H).

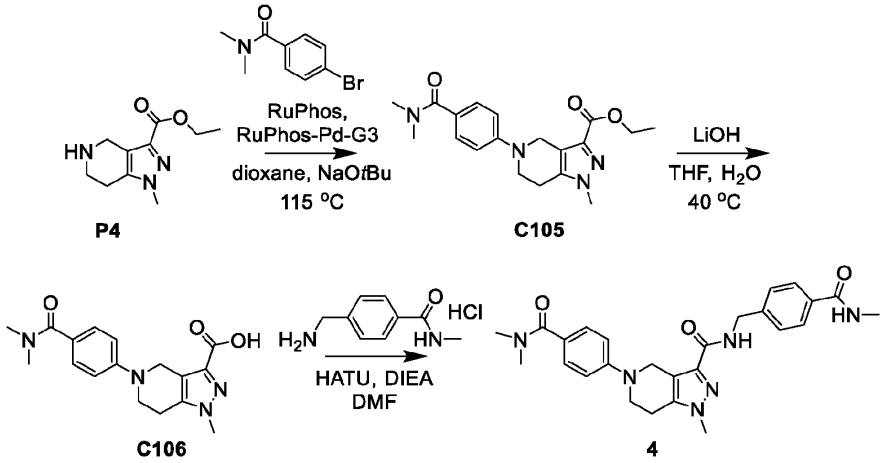
Step 3. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(3)**

The reaction was conducted in two batches and then combined for purification. To a solution of **C104** (0.100 g, 0.291 mmol) in DMSO (3.0 mL) was added HOPO (97.1 mg, 0.874 mmol), DIEA (0.188 g, 1.46 mmol), and EDCI (0.134 g, 0.699 mmol) to form the first batch. The reaction mixture of the first batch was stirred at 40 °C for 15 min before **P11** (73.6 mg, 0.320 mmol) was added. The suspension of the first batch was stirred at 40 °C for 2 h.

The reaction mixture of the first batch was combined with a second batch of the same reaction utilizing **C104** (0.563 g, 1.64 mmol). The combined reaction was purified by reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (NH_4OH-NH_4HCO_3), 3 to 43% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 60 mL/min) and lyophilized to provide **3** (0.467 g, 46.7% yield). (LC/MS) m/z $(M+H)^+$ = 519.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, 1H), 7.62 (dd, 1H), 7.35 (d, 2H), 7.31- 7.27 (m, 2H), 7.09 (t, 1H), 6.77 (d, 1H), 6.31 (s, 1H), 4.75 (s, 2H), 4.55 (d, 2H), 4.15 (t, 2H), 4.03 (q, 2H), 3.08 (s, 6H), 3.03 (s, 6H), 2.81 – 2.74 (m, 2H), 1.40 (t, 3H).

Example 4

5-(4-(Dimethylcarbamoyl)phenyl)-1-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**4**)



Step 1. Preparation of ethyl 5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C105)**

The reaction was conducted in two batches and then combined for purification. To a solution of **P4** (50.0 mg, 0.239 mmol) and 4-bromo-*N*,*N*-dimethylbenzamide (CAS: 18469-37-9, 54.5 mg, 0.239 mmol) in dioxane (3.0 mL) was added RuPhos (11.2 mg, 0.0239 mmol), RuPhos Pd G3 (20.0 mg, 0.0239 mmol) and NaO*t*Bu (45.9 mg, 0.478 mmol) at room temperature to form the first batch. The reaction mixture of the first batch was degassed with nitrogen for 1 min and heated at 115 °C for 20 h.

The first batch's reaction mixture was combined with the second batch of the same reaction utilizing **P4** (0.400 g, 1.91 mmol). The combined reaction was purified by HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% NH_4OH-NH_4HCO_3), 6 to 46% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **C105** (50.0 mg, 6.53% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 357.2.

Step 2. Preparation of 5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(C106)**

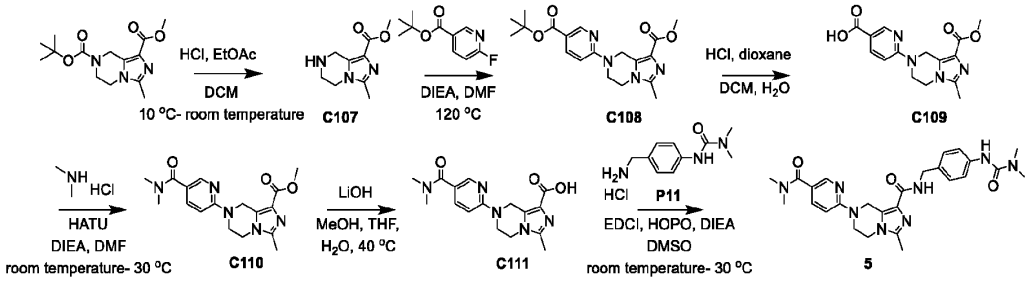
To a solution of **C105** (50.0 mg, 0.140 mmol) in THF (3.0 mL) and H_2O (0.5 mL) was added LiOH (17.7 mg, 0.421 mmol) at room temperature and then stirred at 40 °C for 16 h. The reaction was concentrated *in vacuo,* washed with H_2O (2 x 10 mL), and then acidified with 2M HCl until pH= 5-6; the resulting solid was filtered to provide **C106** (46.0 mg, 89.8% yield) as a white solid. This was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 329.2.

Step 3. Preparation of 5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**4**)

To a solution of **C106** (46.0 mg, 0.140 mmol) in DMF (5.0 mL) was added HATU (79.9 mg, 0.210 mmol), DIEA (54.3 mg, 0.420 mmol), and 4-(aminomethyl)-*N*-methylbenzamide hydrochloride (CAS: 1158467-80-1, 28.1 mg, 0.140 mmol). The reaction was stirred at room temperature for 12 h. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 μm, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 8 to 33% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide an impure **4** (25.0 mg) as a white solid. The solid was re-purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 μm, Mobile Phase A: H_2O/Mobile Phase B: ACN (0.05% NH_4OH-NH_4HCO_3), 4 to 44% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **4** (12.8 mg, 19.3% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 475.2. ^{1}H NMR (400 MHz, CD_3OD) δ 7.80 – 7.74 (m, 2H), 7.46 – 7.42 (m, 2H), 7.38 – 7.33 (m, 2H), 7.08 – 7.02 (m, 2H), 4.60 (s, 2H), 4.50 (s, 2H), 3.80 (s, 3H), 3.74 (t, 2H), 3.06 (s, 6H), 2.91 (s, 3H), 2.84 (t, 2H).

Example 5

7-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(5)**



Step 1. Preparation of methyl 3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate hydrochloride **(C107)**

To a solution of 7-(*tert*-butyl) 1-methyl 3-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazine-1,7(8*H*)-dicarboxylate (CAS: 1359655-89-2, 0.190 g, 0.643 mmol) in DCM (5.0 mL) was added 2M HCl in EtOAc (5.0 mL) at 10 °C. The reaction mixture was stirred at room temperature for 16 h. The resulting white suspension was concentrated *in vacuo* to provide the **C107** (0.149 g, crude) as a white solid. This was used in the next step without further purification. ^{1}H NMR (400 MHz, CD_3OD) δ 4.80 (s, 2H), 4.51 (t, 2H), 4.00 (s, 3H), 3.84 (t, 2H), 2.71 (s, 3H).

Step 2. Preparation of methyl 7-(5-(*tert*-butoxycarbonyl)pyridin-2-yl)-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate **(C108)**

A mixture of **C107** (90.0 mg, 0.388 mmol), *tert*-butyl 6-fluoronicotinate (CAS: 676560-01-3, 152 mg, 0.777 mmol), and DIEA (251 mg, 1.94 mmol) in DMF (4.0 mL) was stirred at 120 °C for 5 h. The light brown reaction mixture was concentrated *in vacuo,* and the residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE) to provide **C108** (87.0 mg, 60.0% yield) as an off-white solid. (LC/MS) m/z $(M+H)^+$ = 373.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80- 8.78 (m, 1H), 8.08 (dd, 1H), 6.75 (d, 1H), 5.00 (s, 2H), 4.31 (t, 2H), 4.02 (t, 2H), 3.93 (s, 3H), 2.43 (s, 3H), 1.58 (s, 9H).

Step 3. Preparation of 6-(1-(methoxycarbonyl)-3-methyl-5,6-dihydroimidazo[1,5-*a*]pyrazin-7(8*H*)-yl)nicotinic acid hydrochloride **(C109)**

To a solution of **C108** (87.0 mg, 0.234 mmol) in DCM (2.0 mL) and 2M HCl in dioxane (2.0 mL) was added H_2O (0.1 mL), then the reaction was stirred for 6 h at room temperature. The light-yellow reaction was concentrated in vacuo and then dried under high vacuum for 3 h to provide **C109** (73.9 mg, crude) as a light brown residue. This was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 317.1.

Step 4. Preparation of methyl 7-(5-(dimethylcarbamoyl)pyridin-2-yl)-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate **(C110)**

To a solution of **C109** (73.0 mg, 0.231 mmol) in DMF (5.0 mL) was added HATU (0.132 g, 0.346 mmol), DIEA (0.149 g, 1.15 mmol), and dimethylamine hydrochloride (CAS: 506-59-2; 28.2 mg, 0.346 mmol) at room temperature. The mixture was stirred at room temperature for 4 h, then heated to 30 °C and stirred for 16 h. The reaction mixture was concentrated *in vacuo* then the residue was purified by column chromatography (silica gel, 0-100% PE: EtOAc to 3.3% MeOH: DCM to provide **C110** (71.0 mg, 78.9% yield) as an off-white solid.

Step 5. Preparation of 7-(5-(dimethylcarbamoyl)pyridin-2-yl)-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylic acid **(C111)**

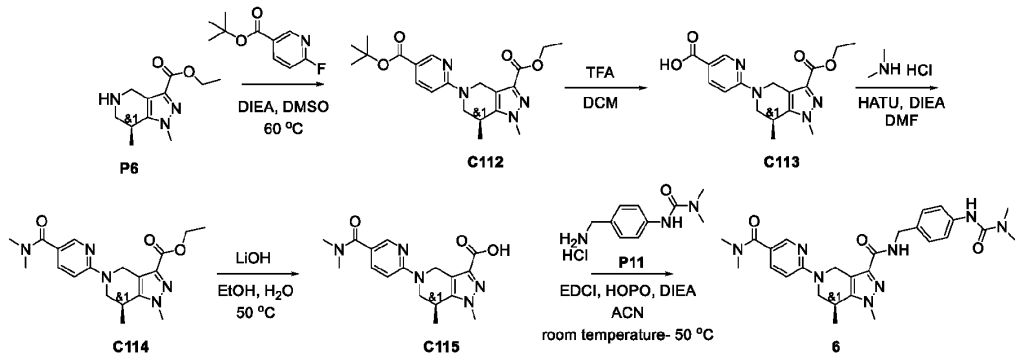
To a solution of **C110** (71.0 mg, 0.207 mmol) in THF (5.0 mL), MeOH (0.5 mL), H_2O (1.0 mL) was added LiOH (15.5 mg, 0.369 mmol) at room temperature. The reaction was stirred at 40 °C for 4 h and then acidified with formic acid to pH= 5. The resulting mixture was concentrated *in vacuo and* then purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 0 to 16% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **C111** (41.0 mg, 60.2% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 330.1.

Step 6. Preparation of 7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(5)**

A mixture of **C111** (40.0 mg, 0.121 mmol), HOPO (40.5 mg, 0.364 mmol), EDCI (55.9 mg, 0.291 mmol), and DIEA (78.5 mg, 0.607 mmol) in DMSO (2.0 mL) was stirred at room temperature for 20 min. **P11** (30.7 mg, 0.134 mmol) was added, and the light brown reaction mixture was stirred at 30 °C for 3 h and 30 min. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 0 to 36% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **5** (28.4 mg, 46.4% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 505.4. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.29- 8.26 (m, 1H), 8.21- 8.15 (m, 2H), 7.69 (dd, 1H), 7.40– 7.35 (m, 2H), 7.17- 7.13 (m, 2H), 6.95 (d, 1H), 5.02 (s, 2H), 4.32 (d, 2H), 4.09– 3.98 (m, 4H), 2.97 (s, 6H), 2.90 (s, 6H), 2.28 (s, 3H).

Example 6

rac-(*R*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**6**)



Step 1: Preparation of *rac*-ethyl (*R*)-5-(5-(*tert*-butoxycarbonyl)pyridin-2-yl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C112**)

To a solution of **P6** (0.426 g, 1.64 mmol), *tert*-butyl 6-fluoronicotinate (CAS: 676560-01-3, 0.356 g, 1.80 mmol) in DMSO (3.4 mL) was added DIEA (1.06 g, 8.20 mmol). The reaction mixture was stirred at 60 °C for 16 h, poured into H_2O (60 mL), and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (2 x 10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography (silica gel, 0-100% EtOAc: heptane) to provide **C112** (0.566 g, 86.2% yield) as a white crystal solid. (LC/MS) m/z $(M+H)^+$ = 401.40. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, 1H), 8.01 (dd, 1H), 6.69 (dd, 1H), 4.95 (d, 1H), 4.72 (dd, 1H), 4.50 – 4.36 (m, 3H), 3.89 (s, 3H), 3.46 (dd, 1H), 3.13- 3.05 (m, 1H), 1.57 (s, 9H), 1.43 (t, 3H), 1.28 (d, 3H).

Step 2: Preparation of *rac-(R)*-6-(3-(ethoxycarbonyl)-1,7-dimethyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinic acid (**C113**)

TFA (2.81 g, 24.7 mmol) was added to a stirred solution of **C112** (0.353 g, 0.881 mmol) in DCM (8.0 mL). The reaction was stirred at room temperature for 4 h and then concentrated *in vacuo*. The resulting gum was sonicated with heptane to yield a solid. The solvent was concentrated *in vacuo* then the white solid was dissolved in EtOAc and concentrated *in vacuo* to provide **C113** (0.304 g, crude) as an off-white solid. This was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 345.40.

Step 3: Preparation of *rac*-ethyl (*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C114**)

A mixture of **C113** (0.304 g, 0.883 mmol), dimethylamine hydrochloride (CAS: 506-59-2; 86.4 mg, 1.06 mmol), HATU (0.369 g, 0.971 mmol), and DIEA (0.342 g, 2.65 mmol) in DMF (1.2 mL) was stirred at room temperature for 4 h. The reaction mixture was quenched with H_2O (30 mL) and extracted with MeOH in DCM (1:9; 4 x 100 mL). The combined organic layer was dried over Na_2SO_4 and then concentrated *in vacuo*. The residue was purified twice by column chromatography. The first purification was by column chromatography (silica gel, 0-100% EtOAc: heptane), and the second purification was by column chromatography (silica gel, 0-15% MeOH: DCM) to provide **C114** (0.208 g, 63.4% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 372.40. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32-8.30 (m, 1H), 7.65 (dd, 1H), 6.74 (d, 1H), 4.92 (d, 1H), 4.58 (dd, 1H), 4.46 – 4.35 (m, 3H), 3.90- 3.86 (m, 3H), 3.74 – 3.64 (m, 1H), 3.46 (dd, 1H), 3.09 (s, 6H), 1.44 – 1.38 (m, 3H), 1.29 (d, 3H).

Step 4: Preparation of *rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C115**)

A flask was charged with **C114** (0.106 g, 0.285 mmol), EtOH (2.3 mL), H_2O (0.9 mL), and LiOH (85.5 mg, 1.14 mmol) and then heated to 50 °C. The reaction mixture became a solution and was stirred at 50 °C for 1 h and 40 min. The reaction was acidified with 12.1M HCl (0.123 g, 3.37 mmol) then concentrated *in vacuo* and dried further under high vacuum to provide **C115** (0.110 g, crude) as a white solid. This was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 344.40.

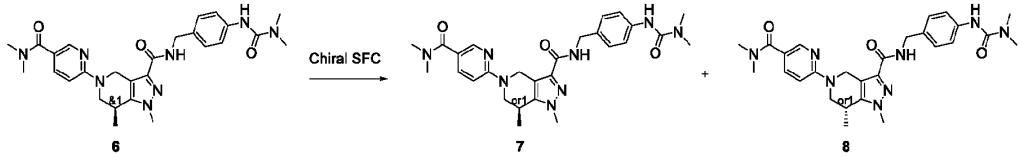
Step 5: Preparation of *rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**6**)

To a solution of **C115** (0.110 g, 0.348 mmol) in ACN (1.7 mL) was added HOPO (46.4 mg, 0.417 mmol) and EDCI (0.233 g, 1.22 mmol). The reaction was heated to 50 °C and stirred for 2 h and 20 min. The solution was cooled to room temperature, and DIEA (0.180 g, 1.39 mmol) was added to give a clear yellow solution. **P11** (87.9 mg, 0.383 mmol) was added to the

reaction and stirred for 1 h at room temperature. The reaction was concentrated *in vacuo* to give an oil, then dissolved in DCM for purification by column chromatography (silica gel, 0-20% MeOH: DCM) to give an impure **6** (65.0 mg) as a yellow oil. The yellow oil was purified again by reverse phase HPLC (Prep PG-45 MOD10 column, Mobile Phase A: H_2O with 2% ACN/ Mobile Phase B: ACN, 5 to 60% of Mobile Phase B over 20 min, 95% of Mobile Phase B hold 5 min, flow rate: 30 mL/min) to provide **6** (34.6 mg, 19.2% yield). (LC/MS) m/z $(M+H)^+$ = 519.2. ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, 1H), 7.62 (dd, 1H), 7.37 – 7.32 (m, 2H), 7.28 – 7.24 (m, 2H), 7.08 (t, 1H), 6.76 (d, 1H), 6.39 (s, 1H), 4.93 (d, 1H), 4.65 – 4.43 (m, 5H), 3.79 (s, 3H), 3.47 (dd, 1H), 3.08 (s, 6H), 3.02 (s, 6H), 1.28 (d, 3H).

Examples 7 and 8

rel-(*R or S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**7**) and (**8**)

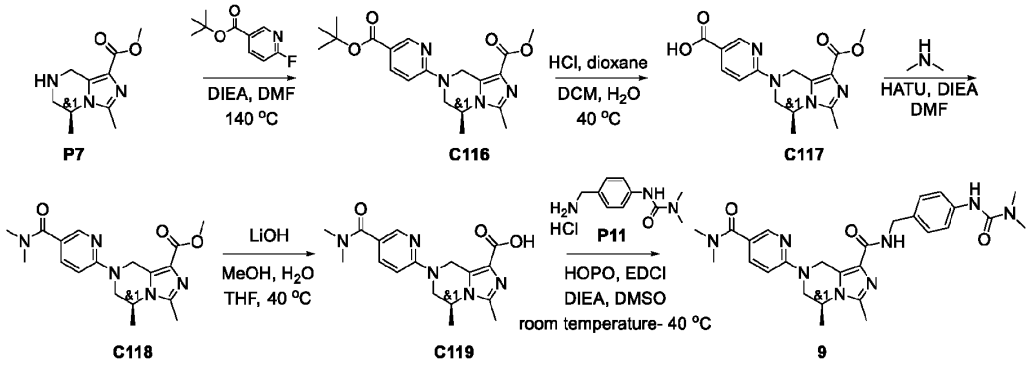


Step 1. Preparation of *rel*-(*R or S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**7**) and (**8**)

Chiral SFC purification of compound **6** (44 mg, 0.085 mmol) [Column: Phenomenex Cellulose-1 250 mm x 10 mm x 5 µm; Mobile phase: 60% CO_2/ 40% (1:1 MeOH/ ACN); flow rate: 25 mL/ min; backpressure: 100 bar; column temperature: 40 °C] provided the first eluting isomer as **7** (4.887 min, 22 mg, 50% yield, 100% ee): (LC/MS) m/z $(M+H)^+$ = 519.3 and the second eluting isomer as **8** (5.377 min, 22 mg, 50% yield, 100% ee): (LC/MS) m/z $(M+H)^+$ = 519.4.

Example 9

rac-(*R*)-7-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide formate (**9**)



Step 1: Preparation of *rac*-methyl (*R*)-7-(5-(*tert*-butoxycarbonyl)pyridin-2-yl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate (**C116**)

A mixture of **P7** (0.111 g, 0.452 mmol), *tert*-butyl 6-fluoronicotinate (CAS: 676560-01-3, 0.223 g, 1.13 mmol), and DIEA (0.292 g, 2.26 mmol) in DMF (5.0 mL) was stirred at 140 °C for 2 h. The light brown reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE then 2% MeOH: EtOAc) to provide **C116** (45.0 mg, 25.7% yield) as a light brown solid. (LC/MS) m/z $(M+H)^+$ = 387.1.

Step 2. Preparation of *rac*-(*R*)-6-(1-(methoxycarbonyl)-3,5-dimethyl-5,6-dihydroimidazo[1,5-*a*]pyrazin-7(8*H*)-yl)nicotinic acid hydrochloride (**C117**)

To a solution of **C116** (45.0 mg, 0.116 mmol) in DCM (3.0 mL) and 2M HCl in dioxane (10.0 mL) was added H_2O (0.02 mL) at room temperature. The reaction was stirred at 40 °C for 2 h and then concentrated *in vacuo* to provide **C117** (42.7 mg, crude) as an off-white solid. This was used in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 331.1.

Step 3. Preparation of *rac*-methyl (*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate (**C118**)

The reaction was conducted in three batches and then combined for purification. To a solution of **C117** (53.0 mg, 0.144 mmol) in DMF (3.0 mL) was added HATU (82.4 mg, 0.217 mmol), DIEA (93.4 mg, 0.722 mmol) and dimethylamine hydrochloride (CAS: 506-59-2; 17.7 mg, 0.217 mmol) at room temperature and then heated to 40 °C and stirred for 16 h. The light brown reaction of the first batch was combined with the second batch of the same reaction utilizing **C117** (42.0 mg, 0.116 mmol) and the third batch of the same reaction utilizing **C117** (70.0 mg, 0.191 mmol). The combined reaction was concentrated *in vacuo* then purified by column chromatography (silica gel; 0-100% EtOAc: PE then 2.5% MeOH: EtOAc) to provide **C118** (75.0 mg, 41.9% yield) as a light brown solid. (LC/MS) m/z $(M+H)^+$ = 358.1.

Step 4. Preparation of *rac*-(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylic acid (**C119**)

The reaction was conducted in two batches and then combined for purification. To a solution of **C118** (75.0 mg, 0.210 mmol) in THF (4.0 mL), MeOH (1.0 mL), and H_2O (2.0 mL) was added LiOH (17.6 mg, 0.420 mmol) at room temperature, which was then heated at 40 °C for 2 h. Another portion of LiOH (8.8 mg, 0.21 mmol) was added and stirred at 40 °C for 3 h.

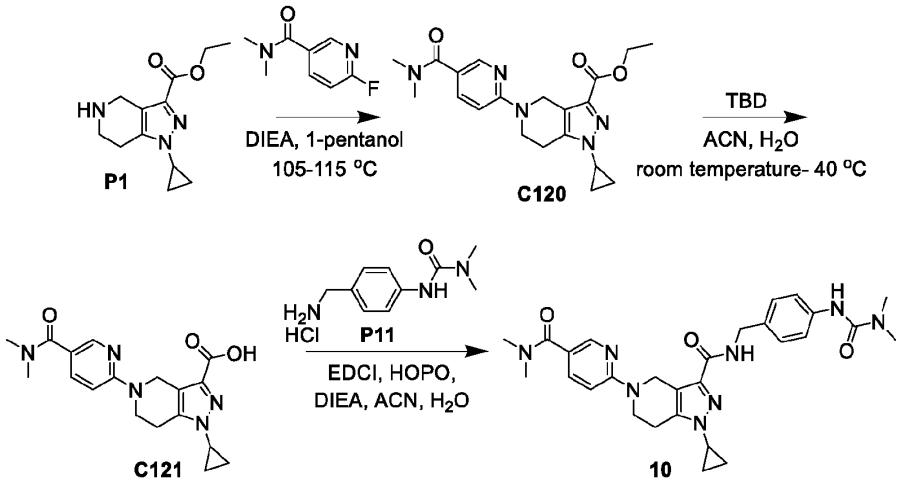
The reaction of the first batch was combined with the second batch of the same reaction utilizing **C118** (33.0 mg, 0.0923 mmol), then acidified with formic acid to pH=~5 and concentrated *in vacuo*. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 0 to 25% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **C119** (59.0 mg, 56.7% yield) as a light brown solid. (LC/MS) m/z $(M+H)^+$ = 344.1.

Step 5. Preparation of *rac*-(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide formate (**9**)

A mixture of **C119** (59.0 mg, 0.172 mmol), HOPO (57.3 mg, 0.515 mmol), EDCI (79.1 mg, 0.412 mmol) and DIEA (111 mg, 0.859 mmol) in DMSO (3.0 mL) was stirred for 30 min at 40 °C, then **P11** (59.2 mg, 0.258 mmol) was added at room temperature. The light brown reaction mixture was stirred at 40 °C for 3 h and 30 min then the residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 0 to 39% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **9** (58.2 mg, 43.2% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 519.5. ^{1}H NMR (400 MHz, CD_3OD) δ 8.31 (d, 1H), 7.74 (dd, 1H), 7.36-7.30 (m, 2H), 7.26 (d, 2H), 6.93 (d, 1H), 5.39 (d, 1H), 4.67- 4.41 (m, 5H), 3.41 (dd, 1H), 3.10 (s, 6H), 3.04- 2.99 (m, 6H), 2.41 (s, 3H), 1.40 (d, 3H).

Example 10

1-Cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide trifluoroacetate **(10)**



Step 1. Preparation of ethyl 1-cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C120)**

To a solution of **P1** (0.070 g, 0.26 mmol) in 1-pentanol (1 mL) and DIEA (0.20 g, 1.5 mmol) was added 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 65 mg, 0.39 mmol). The reaction mixture was heated at 105 °C for 24 h, then the temperature was increased to 115 °C and stirred for 23 h. The reaction mixture was concentrated *in vacuo* and then dissolved with DCM. The solution was purified by column chromatography (silica gel, 0-5% MeOH: DCM) to provide **C120** (0.10 g, crude) as a yellow oil. The oil was used directly in the next step without further purification.

Step 2. Preparation of 1-cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C121)**

To a solution of **C120** (99 mg, 0.26 mmol) in ACN (1 mL) and H_2O (93 µL) was added TBD (0.11 g, 0.77 mmol) and then stirred for 40 min at room temperature followed by 40 °C for 2 h. The reaction was then cooled to room temperature, and 12.1M HCl (24 mg, 0.65 mmol) was added. The acidic reaction mixture was concentrated *in vacuo* to provide **C121** (0.090 g, crude) as a yellow oil. The oil was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 356.2.

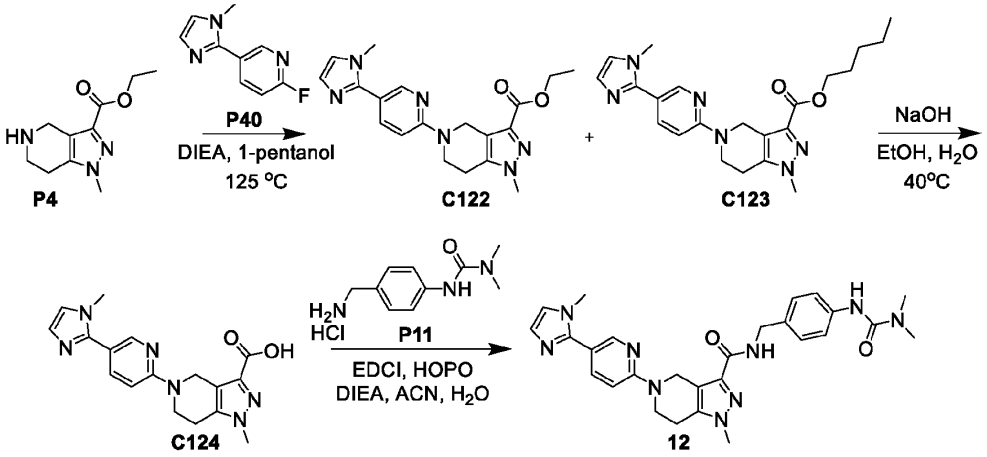
Step 3. Preparation of 1-cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide trifluoroacetate **(10)**

To a solution of **C121** (0.090 g, 0.25 mmol) in ACN (1.0 mL) and H_2O (0.2 mL) was added HOPO (34 mg, 0.30 mmol) and EDCI (78 mg, 0.41 mmol). To the reaction mixture was added an additional portion of EDCI (78 mg, 0.41 mmol) and then was stirred at room temperature for 20 min before DIEA (98 mg, 0.76 mmol) and **P11** (0.070 g, 0.30 mmol) were

added. The suspension was stirred at room temperature for 30 min and then was concentrated *in vacuo*. The residue was diluted with DMSO then acidified with TFA and purified with reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/ Mobile Phase B: ACN (0.05% TFA), 5 to 95% of Mobile Phase B over 9 min, 95% of Mobile Phase B hold 1 min, flow rate= 25 mL/min) and lyophilized to provide **10** (24 mg, 18% yield). (LC/MS) m/z $(M+H)^+$ = 531.5. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.22-8.21 (m, 2H), 7.68 (dd, 1H), 7.40 – 7.34 (m, 2H), 7.15 (d, 2H), 6.96 (d, 1H), 4.75 (s, 2H), 4.32 (d, 2H), 3.96 (t, 2H), 3.56 (tt, 1H), 2.97 (s, 6H), 2.91-2.86 (m, 8H), 1.12-1.05 (m, 2H), 1.01 – 0.95 (m, 2H).

Example 12

N-(4-(3,3-Dimethylureido)benzyl)-1-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(12)**



Step 1. Preparation of ethyl 1-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C122)** and pentyl 1-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C123)**

To a suspension of **P4** (0.60 g, 2.4 mmol) in 1-pentanol (5 mL) was added DIEA (1.9 g, 15 mmol) and **P40** (0.47 g, 2.7 mmol), then heated at 125 °C for 20 h. The reaction mixture was checked by LCMS which showed 30% of **C122** (LC/MS) m/z $(M+H)^+$ = 367.3 and 32% of **C123** at (LC/MS) m/z $(M+H)^+$ = 409.3 was formed due to transesterification with 1-pentanol. The suspension was concentrated *in vacuo* then dissolved in DCM and heptane. The solution was purified by column chromatography (silica gel, 0-10% MeOH: DCM) to form a mixture of **C122** and **C123** (1.1 g, crude) as a brown oil. The brown oil was used directly in the next step without further purification.

Step 2. Preparation of 1-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C124)**

To a reaction mixture of **C122** and **C123** (0.80 g, 2.2 mmol) in EtOH (6 mL) and H_2O (4 mL) was added NaOH (0.35 g, 8.7 mmol) then stirred at 40 °C for 50 min. The suspension was concentrated *in vacuo* and acidified with 12.1M HCl (0.40 g, 11 mmol) to pH~1. The acidic reaction mixture was extracted with DCM then the organic layer was concentrated *in vacuo* to form **C124** (0.30 g, crude) as a brown oil. The oil was used directly in the next step without further purification.

Step 3. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(12)**

To a reaction mixture of **C124** (0.30 g, 0.89 mmol) in ACN (3.0 mL) and H_2O (0.5 mL) was added HOPO (0.12 g, 1.1 mmol) and EDCI (0.27 g, 1.4 mmol). The suspension was stirred at room temperature for 35 min before adding DIEA (0.34 g, 2.7 mmol) and **P11** (0.24 g, 1.1 mmol). The reaction mixture was stirred at room temperature for 30 min and then was concentrated *in vacuo*. The residue was split into two portions for purification.

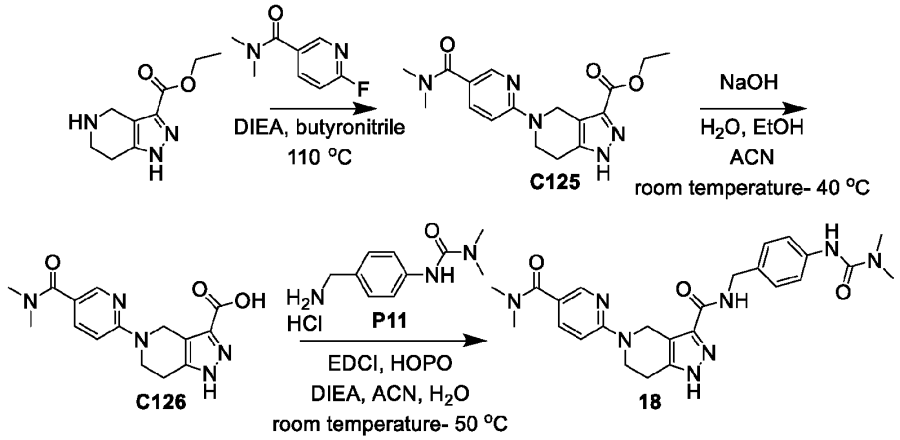
The first portion of the residue was diluted with DMSO and then purified with reverse-phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/ Mobile Phase B: ACN (0.05% TFA), 5 to 95% of Mobile Phase B over 9 min, 95% of Mobile Phase B hold 1 min, flow rate = 25 mL/min) and lyophilized to provide **12** (8.5 mg).

The second portion of the residue was diluted with DCM and then purified by column chromatography (silica gel, 0-5% MeOH: DCM) to provide an impure residue. The impure residue was diluted with MeOH then purified by SFC (Princeton Methanesulfamide Column 250 mm x 30 mm x 5 µm, 70% CO_2/ 30% MeOH (0.2% 7N NH_3 in MeOH), backpressure= 100 bar, temperature= 40 °C, flow rate= 80 mL/min) to provide **12** (62 mg) as a tan solid.

The two purified batches were combined to form **12** (0.070 g, 15% yield) as a solid. (LC/MS) m/z $(M+H)^+$ = 514.4. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.43 (d, 1H), 8.22 (s, 1H), 7.84 (dd, 1H), 7.42 – 7.34 (m, 2H), 7.22 (s, 1H), 7.16 (d, 2H), 7.01 – 6.93 (m, 2H), 4.77 (s, 2H), 4.32 (d, 2H), 3.96 (t, 2H), 3.76 (s, 3H), 3.71 (s, 3H), 2.90 (s, 6H), 2.80 (t, 2H).

Example 18

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(18)**



Step 1. Preparation of ethyl 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C125**)

To a reaction mixture of ethyl 4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride (CAS: 1211512-51-4; 0.380 g, 1.64 mmol) in butyronitrile (10 mL) and DIEA (0.848 g, 6.56 mmol) was added 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3, 0.290 g, 1.72 mmol) then stirred at 110 °C for 23 h. The solution was concentrated *in vacuo* and then redissolved in DCM. The solution was purified by column chromatography (silica gel, 0-7% MeOH: DCM) to provide **C125** (0.439 g, 80.0% yield) as a yellow oil. (LC/MS) m/z $(M+H)^+$ = 344.3.

Step 2. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C126**)

To a solution of **C125** (0.439 g, 1.28 mmol) in ACN (5 mL), H_2O (2 mL), and EtOH (5 mL) was added NaOH (102 mg, 2.56 mmol). The solution was stirred at room temperature for 2 h then heated to 40 °C and stirred for 3 h and 20 min. The reaction solution was acidified with 12.1M HCl (0.140 g, 3.84 mmol) then concentrated *in vacuo* to provide **C126** (0.384 g, crude) as an off-white solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 316.3.

Step 3. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(18)**

To a solution of **C126** (0.200 g, 0.634 mmol) in ACN (5 mL) was added HOPO (84.6 mg, 0.761 mmol) and EDCI (0.195 g, 1.01 mmol). The reaction mixture was stirred at 50 °C for 20 min, then H_2O (1 mL), DIEA (0.246 g, 1.90 mmol), and **P11** (0.160 g, 0.698 mmol) were added.

The reaction mixture was stirred at room temperature for 15 min then concentrated *in vacuo*. The residue was dissolved in DCM and then purified by column chromatography (silica gel, 0-15% MeOH: DCM) to form an impure **18** (0.386 g).

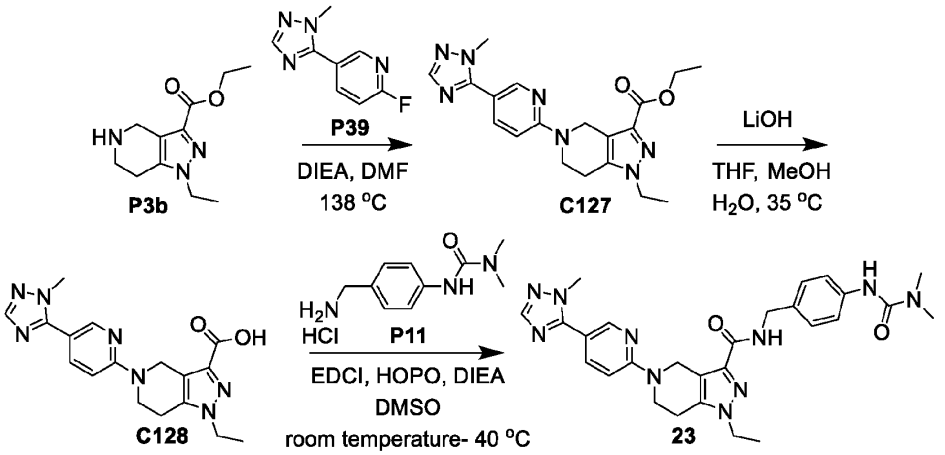
A portion of the impure **18** (0.0400 g) was purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 5 to 95% of Mobile Phase B over 9 min, 95% oh Mobile Phase B hold 1 min, flow rate = 25 mL/min) and lyophilized to provide **18** (9.90 mg).

The remaining of the portion of the impure **18** (0.346 g) was purified by SFC (Princeton CN 250 mm x 30 mm x 5 µm, 70% CO_2/ 25% MeOH (7N NH_3 in MeOH), backpressure = 100 bar, temperature = 40 °C, flow rate = 80 mL/min) to provide **18** (55.9 mg).

The two final batches were combined to provide **18** (65.8 mg, 21.1% yield) as a solid. (LC/MS) m/z $(M+H)^+$ = 491.4. ^{1}H NMR (400 MHz, CD_3OD) δ 8.26 (d, 1H), 7.67 (dd, 1H), 7.35-7.25 (m, 4H), 6.89 (d, 1H),4.78 (s, 2H), 4.50 (s, 2H), 4.05 (t, 2H), 3.08 (s, 6H), 3.00 (s, 6H), 2.84 (t, 2H).

Example 23

N-(4-(3,3-Dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(23)**



Step 1. Preparation of ethyl 1-ethyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C127)**

To a reaction mixture of **P3b** (0.150 g, 0.842 mmol) and **P39** (0.219 g, 0.842 mmol) in DMF (4.2 mL) was added DIEA (0.544 g, 4.21 mmol) and then stirred at 138 °C for 48 h. The suspension was diluted with EtOAc (30 mL), and then the organic layer was washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried with Na_2SO_4 and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-58% THF: PE) to provide **C127** (0.200 g, 62.3% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 382.2.

Step 2. Preparation of 1-ethyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C128)**

To a solution of **C127** (0.200 g, 0.524 mmol) in THF (2.0 mL), H_2O (0.5 mL), and MeOH (0.5 mL) was added LiOH (66.0 mg, 1.57 mmol) at room temperature. The reaction mixture was heated to 35 °C and stirred for 2 h. The suspension was extracted with EtOAc (2 x 10 mL), and then the combined organic layer was washed with H_2O (10 mL). The aqueous layer was acidified to pH =3 with citric acid, which caused precipitation to form. The suspension was filtered, and then the filter cake was collected and lyophilized to provide **C128** (0.150 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 354.2.

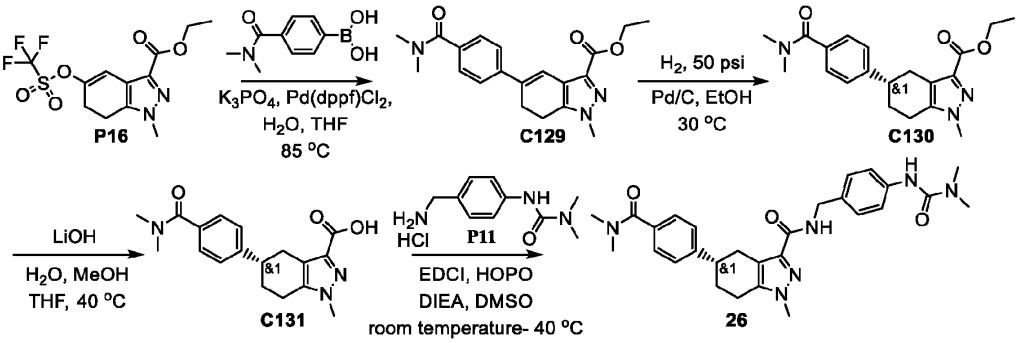
Step 3. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(23)**

The reaction was conducted in two batches and then combined for purification. To a solution of **C128** (0.060 g, 0.17 mmol) in DMSO (1.0 mL) was added HOPO (56 mg, 0.50 mmol), DIEA (0.11 g, 0.85 mmol), and EDCI (78 mg, 0.41 mmol). The reaction mixture was stirred at room temperature for 5 min, and then **P11** (58 mg, 0.25 mmol) was added to form the first batch. The reaction mixture of the first batch was stirred at 40 °C for 2 h.

A second batch of the same reaction was conducted with **C128** (15 mg, 0.043 mmol). The two batches were combined then purified by reverse phase HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (NH_4OH-NH_4HCO_3), 20 to 50% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 3 min, flow rate= 50 mL/min) and lyophilized to provide **23** (62 mg, 55% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 529.3. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.56 (d, 1H), 8.44 (t, 1H), 8.23 (s, 1H), 7.99 – 7.92 (m, 2H), 7.45 – 7.34 (m, 2H), 7.22 – 7.17 (m, 2H), 7.05 (d, 1H), 4.83 (s, 2H), 4.36 (d, 2H), 4.11 (q, 2H), 4.02 (t, 2H), 3.97 (s, 3H), 2.93 (s, 6H), 2.86 (t, 2H), 1.36 (t, 3H).

Example 26

rac-(*R*)-5-(4-(Dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxamide **(26)**



Step 1. Preparation of ethyl 5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-6,7-dihydro-1*H*-indazole-3-carboxylate **(C129)**

Under nitrogen gas, to a mixture of **P16** (0.500 g, 1.41 mmol) and (4-(dimethylcarbamoyl)phenyl)boronic acid (0.409 g, 2.12 mmol) in H_2O (1 mL) and THF (10 mL) was added $Pd(dppf)Cl_2$ (0.103 g, 0.141 mmol) and K_3PO_4 (0.899 g, 4.23 mmol). The reaction mixture was stirred at 85 °C for 16 h and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-62% THF: PE) to provide **C129** (0.470 g, 94.2% yield) as a pink solid. (LC/MS) m/z $(M+H)^+$ = 354.1. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 7.62 – 7.55 (m, 2H), 7.45 – 7.39 (m, 2H), 7.15 – 7.12 (m, 1H), 4.33 – 4.24 (m, 2H), 3.85 – 3.82 (m, 3H), 3.76 – 3.54 (m, 2H), 3.01 – 2.94 (m, 6H), 2.93 – 2.85 (m, 2H), 1.31 (t, 3H).

Step 2. Preparation of *rac*-ethyl (*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxylate **(C130)**

A solution of **C129** (0.050 g, 0.14 mmol) was added in a thick-walled pressure vial in EtOH (5 mL). Pd/C (45 mg, 0.042 mmol) was added to the solution. The vial was evacuated under vacuum then purged with H_2 gas. The reaction mixture was stirred under H_2 atmosphere (50 psi) at 30 °C for 16 h then concentrated *in vacuo* to provide **C130** (45 mg, 89% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 2H), 7.30 – 7.26 (m, 2H), 4.37 (q, 2H), 3.83 (s, 3H), 3.19 (dd, 1H), 3.14 – 2.98 (m, 6H), 2.97 – 2.90 (m, 1H), 2.81 – 2.61 (m, 3H), 2.20 – 2.12 (m, 1H), 2.05 – 1.92 (m, 1H), 1.37 (t, 3H).

Step 3. Preparation of *rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxylic acid **(C131)**

To a solution of **C130** (45 mg, 0.13 mmol) in THF (1.00 mL), H_2O (0.25 mL), and MeOH (0.25 mL) was added LiOH (16 mg, 0.38 mmol). The reaction mixture was stirred at 40 °C for 2 h, diluted with EtOAc (2 x 10 mL), and washed with H_2O (10 mL). The aqueous phase was separated and adjusted with citric acid to pH~3, then extracted with DCM (5 x 50 mL). The combined organic layer was dried with Na_2SO_4 and concentrated *in vacuo* to provide **C131** (35 mg, 84% yield) as a brown solid. (LC/MS) m/z $(M+H)^+$ = 328.1.

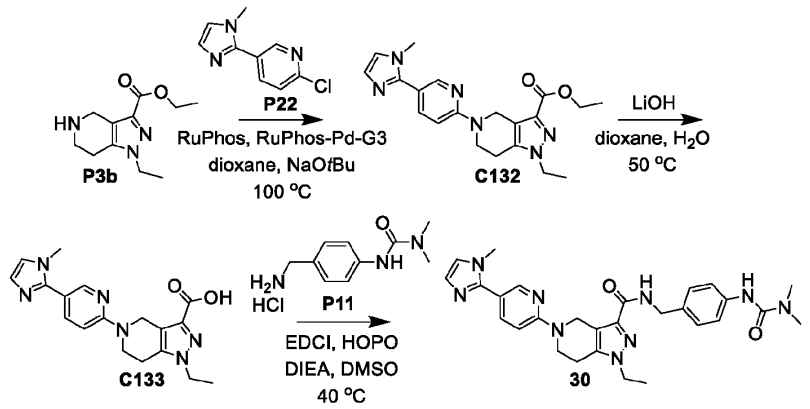
Step 4. Preparation of *rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxamide **(26)**

To a solution of **C131** (35 mg, 0.11 mmol) in DMSO (1 mL) was added HOPO (35 mg, 0.31 mmol), EDCI (49 mg, 0.26 mmol), and DIEA (69 mg, 0.53 mmol). The reaction mixture was stirred at room temperature for 5 min, and then **P11** (37 mg, 0.16 mmol) was added. The suspension was stirred at 40 °C for 1 h then was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 14 to 44% of Mobile Phase B over 10 min, 100% of Mobile Phase B hold 3 min, flow rate= 50

mL/min) and lyophilized to provide **26** (11 mg, 20.% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 503.4. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.31 (t, 1H), 8.22 (s, 1H), 7.42 – 7.32 (m, 6H), 7.17 – 7.11 (m, 2H), 4.31 (d, 2H), 3.76 (s, 3H), 3.14 – 3.04 (m, 1H), 3.00 – 2.89 (m, 12H), 2.85 – 2.58 (m, 4H), 2.12 – 1.88 (m, 2H).

Example 30

N-(4-(3,3-Dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**30**)



Step 1. Preparation of ethyl 1-ethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C132)**

To a solution of **P3b** (0.760 g, 2.93 mmol), **P22** (0.680 g, 3.51 mmol) and NaO*t*Bu (0.843 g, 8.78 mmol) in dioxane (15 mL) was added RuPhos (0.273 g, 0.585 mmol) and RuPhos Pd G3 (0.489 g, 0.585 mmol) at room temperature. The reaction mixture was degassed with nitrogen gas and then stirred at 100 °C for 4 h to provide **C132** (1.11 g, crude) as a solution. The solution was used directly in the next step without further purification. (LC/MS) m/z $(M\text{-ethyl})^+$ = 353.2.

Step 2. Preparation of 1-ethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C133)**

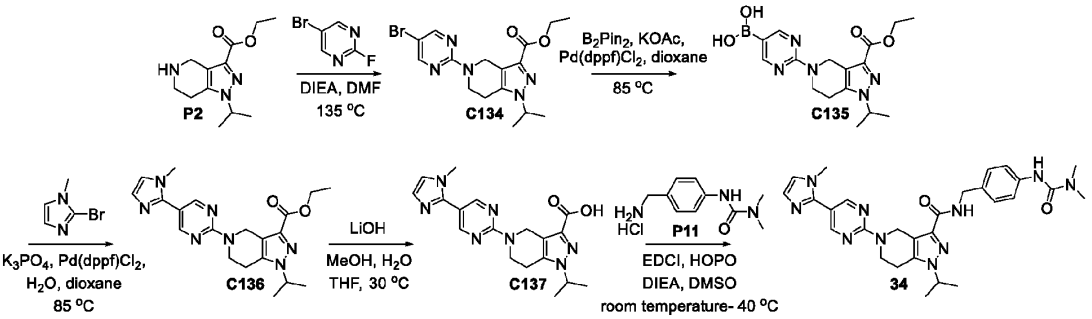
To a solution of **C132** (1.26 g, 3.31 mmol) in dioxane (15 mL) and H_2O (5 mL) was added LiOH (0.397 g,16.6 mmol) at room temperature then stirred at 50 °C for 5 h. The reaction was purified by reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O (0.05% formic acid)/ Mobile Phase B: ACN, 0 to 35% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate= 60 mL/min) and lyophilized to provide **C133** (0.200 g, 17.1% yield) as a yellow solid. (LC/MS) m/z $(M+H)^+$ = 353.1. ^1H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, 1H), 8.22 (s, 1H), 8.02 (dd, 1H), 7.37 (d, 1H), 6.98 (d, 1H), 6.89 (d, 1H), 4.76 (s, 2H), 4.20 – 4.05 (m, 4H), 3.80 (s, 3H), 2.82 (t, 2H), 1.45 (t, 3H).

Step 3. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**30**)

To a solution of **C133** (0.080 g, 0.23 mmol) in DMSO (2 mL) was added EDCI (0.10 g, 0.54 mmol), HOPO (76 mg, 0.68 mmol) and DIEA (0.15 g, 1.1 mmol) and stirred for 30 min at 40 °C then **P11** (78 mg, 0.34 mmol) was added. The reaction was stirred at 40 °C for 1 h. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (0.05% NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 20 to 60% of Mobile Phase B over 15 min, 100% of Mobile Phase B hold 2 min, flow rate= 30 mL/min) and lyophilized to provide **30** (44 mg, 37% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 528.4. ^1H NMR (400 MHz, CD_3OD) δ 8.37 (d, 1H), 7.80 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.30 – 7.26 (m, 2H), 7.15 (d, 1H), 7.01 (d, 1H), 6.98 (d, 1H), 4.78 (s, 2H), 4.50 (s, 2H), 4.16 – 4.04 (m, 4H), 3.74 (s, 3H), 3.01 (s, 6H), 2.85 (t, 2H), 1.41 (t, 3H).

Example 34

N-(4-(3,3-Dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(34)**



Step 1. Preparation of ethyl 5-(5-bromopyrimidin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C134)**

The reaction was conducted in two batches and then combined. To a solution of **P2** (0.541 g, 1.98 mmol) and 5-bromo-2-fluoropyrimidine (CAS: 62802-38-4; 0.350 g, 1.98 mmol) in DMF (5 mL) was added DIEA (1.28 g, 9.89 mmol) and the reaction heated at 135 °C for 16 h to form the first batch. A second batch of the same reaction was conducted with **P2** (77.4 mg, 0.283 mmol). The two batches were combined and diluted with EtOAc (50 mL). The suspension was washed with H_2O (3 x 30 mL) and then brine (20 mL). The organic layer was dried with Na_2SO_4 and then concentrated *in vacuo*. The residue was purified with column chromatography (silica gel, 0-23% EtOAc: PE) to provide **C134** (0.750 g, 84.2% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 394.1. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.50 (s, 2H), 4.85 (s, 2H), 4.56 – 4.46 (m, 1H), 4.29 (q, 2H), 4.05 (t, 2H), 2.81 (t, 2H), 1.39 – 1.35 (m, 6H), 1.31 (t, 3H).

Step 2. Preparation of (2-(3-(ethoxycarbonyl)-1-isopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyrimidin-5-yl)boronic acid **(C135)**

To a reaction mixture of **C134** (0.350 g, 0.888 mmol) and B_2Pin_2 (0.271 g, 1.07 mmol) in dioxane (5 mL) was added KOAc (0.261 g, 2.66 mmol) and $Pd(dppf)Cl_2$ (52.0 mg, 0.0710 mmol). The suspension was purged with nitrogen gas for 3 min and then stirred at 85 °C for 16 h to provide **C135** (0.319 g, crude) as a reaction mixture, which was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 360.0.

Step 3. Preparation of ethyl 1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C136)**

The same reaction was conducted in two batches and then combined. To a reaction mixture of **C135** (0.319 g, 0.888 mmol) and 2-bromo-1-methyl-1*H*-imidazole (0.214 g, 1.33 mmol) in dioxane (2.00 mL) and H_2O (0.25 mL) was added $Pd(dppf)Cl_2$ (65.0 mg, 0.0888 mmol) and K_3PO_4 (0.566 g, 2.66 mmol) to form the first batch. The suspension of the first batch was purged with nitrogen gas then stirred at 85 °C for 2 h.

A second batch of the same reaction was conducted with **C135** (46.0 mg, 0.128 mmol). The two batches were combined and diluted with EtOAc (30 mL). The suspension was washed with H_2O (2 x 20 mL) and then brine (20 mL). The organic layer was dried with Na_2SO_4 and then concentrated *in vacuo*. The residue was purified with column chromatography (silica gel, 0-50% THF: PE) to provide **C136** (0.214 g, 53.1% yield) as a brown oil. (LC/MS) m/z $(M+H)^+$ = 396.2.

Step 4. Preparation of 1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C137)**

To a solution of **C136** (0.214 g, 0.541 mmol) in THF (1.00 mL), H_2O (0.25 mL), and MeOH (0.25 mL) was added LiOH (68.1 mg, 1.62 mmol). The reaction mixture was stirred at 30 °C for 2 h and then extracted with EtOAc (2 x 10 mL). The combined organic layer was washed with H_2O (5 mL). The aqueous layer was adjusted with citric acid to pH=3 and then extracted with DCM (3 x 5 mL). The combined organic layer was dried with Na_2SO_4 and then concentrated *in vacuo*. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 μm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 8 to 48% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate= 60 mL/min) and lyophilized to provide **C137** (90.0 mg, 45.3% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 368.2.

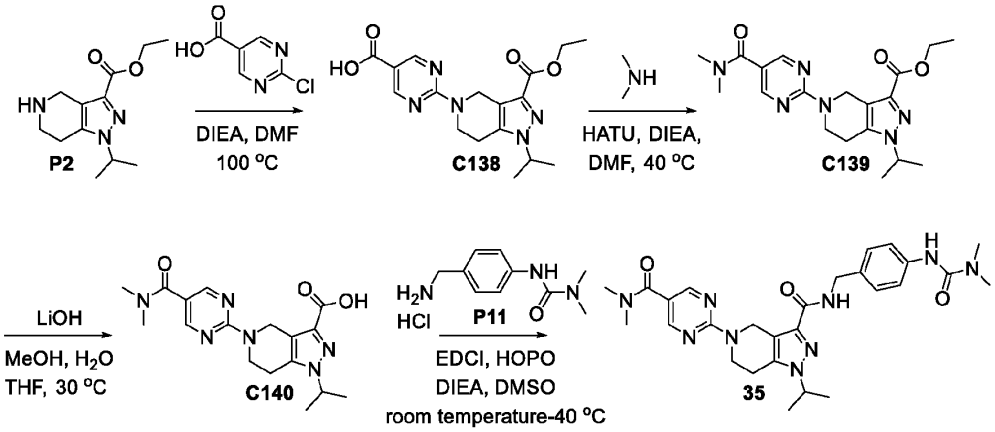
Step 5. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(34)**

The same reaction was conducted in two batches and then combined. To a solution of **C137** (0.070 g, 0.19 mmol) in DMSO (1 mL) was added HOPO (63 mg, 0.56 mmol), EDCI (88 mg, 0.46 mmol), and DIEA (0.12 g, 0.95 mmol). The reaction mixture was stirred at room temperature for 5 min, and then **P11** (66 mg, 0.29 mmol) was added to form the first batch. The suspension of the first batch was stirred at 40 °C for 2 h.

A second batch of the same reaction was conducted with **C137** (0.020 g, 0.054 mmol). The two batches were combined then purified with reverse phase HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 18 to 48% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 3 min, flow rate= 25 mL/min) and lyophilized to provide **34** (68 mg, 51% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 543.5. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.69 (s, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.41 – 7.36 (m, 2H), 7.24 (d, 1H), 7.19 – 7.14 (m, 2H), 6.95 (d, 1H), 4.96 (s, 2H), 4.52 – 4.43 (m, 1H), 4.34 (d, 2H), 4.14 (t, 2H), 3.71 (s, 3H), 2.90 (s, 6H), 2.83 (t, 2H), 1.39 (d, 6H).

Example 35

5-(5-(Dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(35)**



Step 1. Preparation of 2-(3-(ethoxycarbonyl)-1-isopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyrimidine-5-carboxylic acid **(C138)**

To a solution of **P2** (0.350 g, 1.28 mmol) and 2-chloropyrimidine-5-carboxylic acid (CAS: 374068-01-6; 0.203 g, 1.28 mmol) in DMF (5 mL) was added DIEA (0.826 g, 6.39 mmol). The reaction mixture was stirred at 100 °C for 16 h to provide **C138** (0.459 g, crude) as a suspension. The reaction mixture was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 360.2.

Step 2. Preparation of ethyl 5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C139)**

The same reaction was conducted in two batches and then combined. To a solution of **C138** (0.459 g, 1.28 mmol) and dimethylamine hydrochloride (CAS: 506-59-2; 0.156 g, 1.91 mmol) in DMF (6 mL) was added DIEA (0.825 g, 6.39 mmol) and HATU (0.728 g, 1.92 mmol) at room temperature to form the first batch. The reaction mixture of the first batch was stirred at 40 °C for 1 h.

A second batch of the same reaction was conducted with **C138** (39.0 mg, 0.108 mmol). The two batches were combined and diluted with EtOAc (50 mL). The suspension was washed with H_2O (3 x 30 mL) and then brine (30 mL). The organic layer was dried with Na_2SO_4 and then concentrated *in vacuo*. The residue was purified with column chromatography (silica gel, 0-54% THF: PE) to provide **C139** (0.500 g, 89.4% yield) as an off-white solid. (LC/MS) m/z $(M+H)^+$ = 387.3. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.54 (s, 2H), 4.95 (s, 2H), 4.59 – 4.48 (m, 1H), 4.30 (q, 2H), 4.15 (t, 2H), 2.99 (br s, 6H), 2.84 (t, 2H), 1.41 – 1.35 (m, 6H), 1.32 (t, 3H).

Step 3. Preparation of 5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C140)**

The same reaction was conducted in two batches and then combined. To a solution of **C139** (0.180 g, 0.466 mmol) in THF (1.00 mL), H_2O (0.25 mL), and MeOH (0.25 mL) was added LiOH (39.1 mg, 0.932 mmol) to form the first batch. The reaction mixture of the first batch was stirred at 30 °C for 2 h.

A second batch of the same reaction was conducted with **C139** (20.0 mg, 0.0517 mmol). The two batches were combined and extracted with EtOAc (2 x 10 mL). The combined organic layer was washed with H_2O (10 mL). The aqueous layer was adjusted with citric acid to pH=3 and then extracted with DCM (5 x 50 mL). The combined organic layer was dried with Na_2SO_4 and then concentrated *in vacuo* to provide **C140** (0.145 g, crude) as an off-yellow solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 359.3.

Step 4. Preparation of 5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(35)**

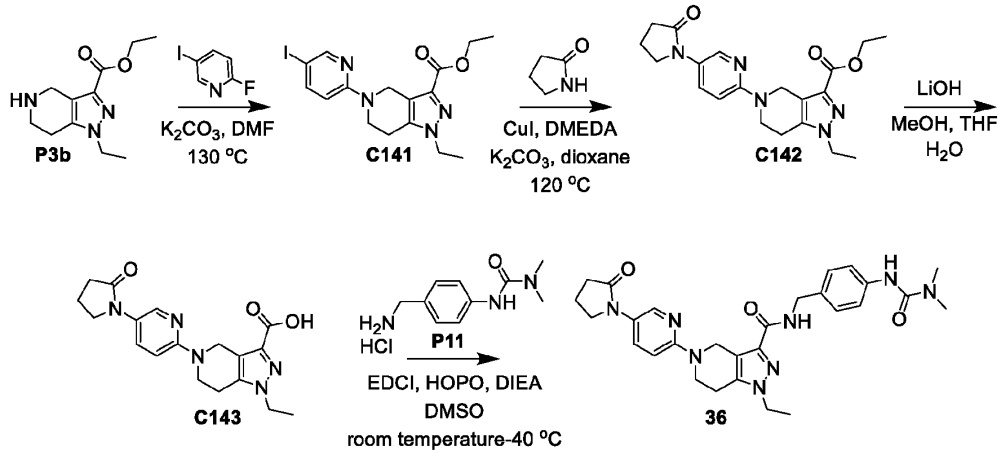
The same reaction was conducted in two batches and then combined. To a solution of **C140** (0.060 g, 0.17 mmol) in DMSO (1 mL) was added HOPO (55 mg, 0.49 mmol), EDCI (77 mg, 0.40 mmol), and DIEA (0.11 g, 0.84 mmol). The reaction mixture was stirred at room temperature for 5 min, and then **P11** (58 mg, 0.25 mmol) was added to form the first batch. The suspension of the first batch was stirred at 40 °C for 2 h.

A second batch of the same reaction was conducted with **C140** (0.020 g, 0.056 mmol). The two batches were combined then purified with reverse phase HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 μm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN,

15 to 45% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 3 min, flow rate= 25 mL/min) and lyophilized to provide **35** (0.040 g, 38% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 534.5. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.51 (s, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.41 – 7.35 (m, 2H), 7.16 (d, 2H), 4.94 (s, 2H), 4.53 – 4.42 (m, 1H), 4.33 (d, 2H), 4.12 (t, 2H), 2.97 (br s, 6H), 2.90 (s, 6H), 2.81 (t, 2H), 1.38 (d, 6H).

Example 36

N-(4-(3,3-Dimethylureido)benzyl)-1-ethyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(36)**



Step 1. Preparation of ethyl 1-ethyl-5-(5-iodopyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C141**)

A reaction mixture of **P3b** (0.803 g, 3.09 mmol), 2-fluoro-5-iodopyridine (CAS: 171197-80-1, 0.896 g, 4.02 mmol), and K_2CO_3 (1.28 g, 9.27 mmol) in DMF (20 mL) was stirred at 130 °C for 21 h. The brown reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica gel, 0- 40% EtOAc: PE) to provide **C141** (0.632 g, 48.0% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 427.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, 1H), 7.68 (dd, 1H), 6.61 – 6.55 (m, 1H), 4.61 (s, 2H), 4.43 (q, 2H), 4.18 – 4.11 (m, 2H), 4.03 (t, 2H), 2.78 (t, 2H), 1.47 – 1.38 (m, 6H).

Step 2. Preparation of ethyl 1-ethyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C142**)

Under nitrogen gas, a reaction mixture of **C141** (0.380 g, 0.891 mmol), pyrrolidine-2-one (0.114 g, 1.34 mmol), CuI (34.0 mg, 0.178 mmol), DMEDA (15.7 mg, 0.178 mmol) and K_2CO_3 (0.370 g, 2.68 mmol) in dioxane (10.0 mL) was heated at 120 °C for 16 h. The suspension was concentrated *in vacuo* and then purified by column chromatography (silica gel, 0-70% THF: PE) to provide **C142** (0.337 g, 98.6% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 384.2.

Step 3. Preparation of 1-ethyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C143**)

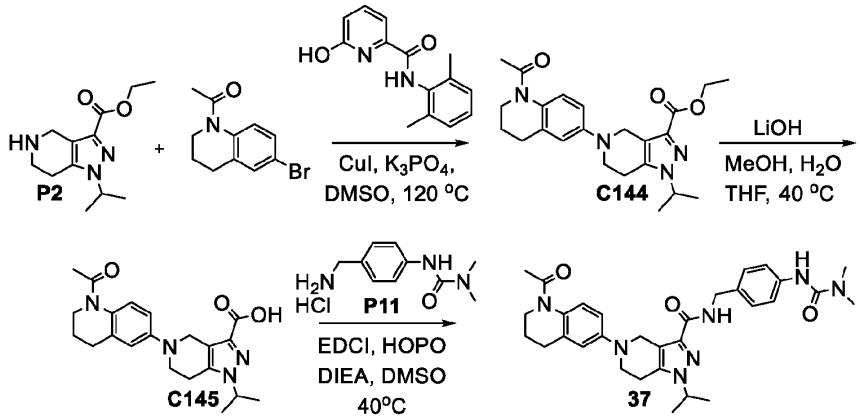
To a solution of **C142** (0.300 g, 0.782 mmol) in THF (5.00 mL), MeOH (1.25 mL) and H_2O (2.50 mL) was added LiOH (49.7 mg, 2.07 mmol) then stirred at room temperature for 1 h. The solution was concentrated *in vacuo* to remove the organic solvents, then the resultant light-yellow aqueous solution was acidified to pH=3-4 with 2N HCl, which caused an off-white solid precipitate to form. The suspension was filtered, and then the filter cake was washed with H_2O (3 x 50 mL) and dried under high *vacuo*. The filter cake was collected and then lyophilized to provide **C143** (0.170 g, 61.1% yield) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) δ 8.29 (d, 1H), 7.82 (dd, 1H), 6.91 (d, 1H), 4.67 (s, 2H), 4.14 (q, 2H), 3.97 (t, 2H), 3.89 – 3.81 (m, 2H), 2.84 (t, 2H), 2.60 – 2.52 (m, 2H), 2.23 – 2.13 (m, 2H), 1.40 (t, 3H).

Step 4. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**36**)

A solution of **C143** (0.080 mg, 0.23 mmol), HOPO (74 mg, 0.66 mmol), EDCI (0.10 g, 0.54 mmol), and DIEA (0.14 g, 1.1 mmol) in DMSO (2.5 mL) was stirred at room temperature for 10 min, then **P11** (62 mg, 0.27 mmol) was added and reaction mixture was stirred at 40 °C for 2 h. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (NH_4OH-NH_4HCO_3), 15 to 55% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate= 30 mL/min) and lyophilized to provide **36** (28 mg, 23% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 531.5. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.42 (t, 1H), 8.30 (d, 1H), 8.23 (s, 1H), 7.90 (dd, 1H), 7.43 – 7.36 (m, 2H), 7.21 – 7.15 (m, 2H), 6.92 (d, 1H), 4.67 (s, 2H), 4.34 (d, 2H), 4.08 (q, 2H), 3.88 (t, 2H), 3.78 (t, 2H), 2.92 (s, 6H), 2.83 – 2.77 (m, 2H), 2.44 (t, 2H), 2.11 – 2.01 (m, 2H), 1.33 (t, 3H).

Example 37

5-(1-Acetyl-1,2,3,4-tetrahydroquinolin-6-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(37)**



Step 1. Preparation of ethyl 5-(1-acetyl-1,2,3,4-tetrahydroquinolin-6-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C144)**

The same reaction was conducted in two batches and then combined. To a solution of **P2** (0.450 g, 1.90 mmol), *N*-(2,6-dimethylphenyl)-6-hydroxypyridine-2-carboxamide (CAS: 1982260-18-3; 0.122 g, 0.506 mmol) and 1-(6-bromo-3,4-dihydroquinolin-1(2*H*)-yl)ethan-1-one (CAS: 22190-40-5; 0.483 g, 1.90 mmol) in DMSO (20 mL) was added K_3PO_4 (1.07 g, 5.06 mmol) and CuI (48.2 mg, 0.253 mmol) at room temperature to form the first batch. The reaction mixture of the first batch was purged with nitrogen gas for 3 min and then stirred at 120 °C for 13 h.

A second batch of the same reaction was conducted with **P2** (50.0 mg, 0.211 mmol). The two batches were combined and then concentrated *in vacuo*. The residue was purified with column chromatography (silica gel, 0-64% EtOAc: PE) to provide **C144** (0.120 g, 15.4% yield) as a yellow solid. (LC/MS) m/z $(M+H)^+$ = 411.1.

Step 2. Preparation of 5-(1-acetyl-1,2,3,4-tetrahydroquinolin-6-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C145)**

To a solution **C144** (0.120 g, 0.292 mmol) in THF (4 mL), MeOH (1 mL), and H_2O (2 mL), LiOH (24.5 mg, 0.585 mmol) was added at room temperature. The reaction mixture was stirred at 40 °C for 1 h and then was acidified with 2M HCl to pH=5. The acidic suspension was concentrated *in vacuo* and then lyophilized to provide an off-white solid. The solid was purified with reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (formic acid)/ Mobile Phase B: ACN, 17 to 57% of Mobile Phase B over 15 min, 100% of Mobile Phase B hold 2 min, flow rate= 30 mL/min) and lyophilized to provide **C145** (70.0 mg, 62.5% yield) as a yellow solid. (LC/MS) m/z $(M+H)^+$ = 383.3. ^{1}H NMR (400 MHz, CD_3OD) δ 7.15 – 7.04 (m, 1H), 6.93 – 6.83 (m, 2H), 4.58 – 4.49 (m, 1H), 4.37 (s, 2H), 3.74 (t, 2H), 3.62 (t, 2H), 2.87 (t, 2H), 2.75 – 2.64 (m, 2H), 2.27 – 2.11 (m, 3H), 2.00 – 1.87 (m, 2H), 1.48 (d, 6H).

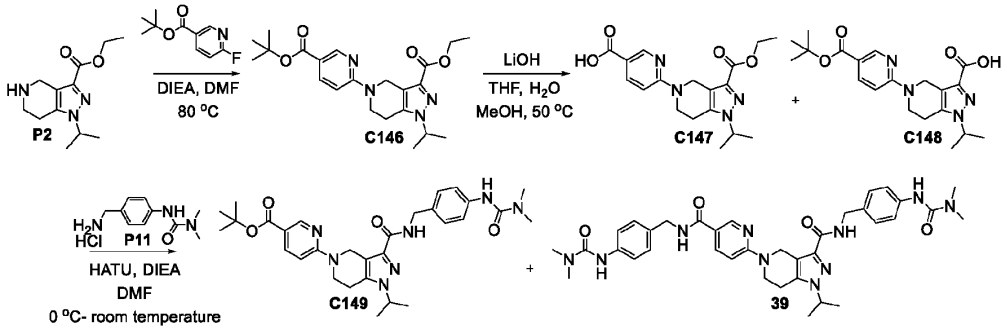
Step 3. Preparation of 5-(1-acetyl-1,2,3,4-tetrahydroquinolin-6-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(37)**

To a reaction mixture of **C145** (0.070 g, 0.18 mmol), HOPO (61 mg, 0.55 mmol), and EDCI (84 mg, 0.44 mmol) in DMSO (2 mL) was added **P11** (0.050 g, 0.22 mmol) and DIEA (0.14 g, 1.1 mmol). The suspension was stirred at room temperature for 10 min, and then the light-brown solution was stirred at 40 °C for 2 h. The light-brown reaction mixture was purified with reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 22 to 62% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min) and lyophilized to provide **37** (0.055 g, 54% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 558.5. ^{1}H NMR (400 MHz, CD_3OD) δ 7.38 – 7.33 (m, 2H), 7.32 – 7.27

(m, 2H), 7.15 – 7.06 (m, 1H), 6.92 (d, 2H), 4.56 – 4.48 (m, 3H), 4.42 (s, 2H), 3.75 (t, 2H), 3.63 (t, 2H), 3.02 (s, 6H), 2.87 (t, 2H), 2.74 – 2.65 (m, 2H), 2.29 – 2.15 (m, 3H), 2.00 – 1.88 (m, 2H), 1.48 (d, 6H).

Example 39

N-(4-(3,3-Dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(39)**



Step 1: Preparation of ethyl 5-(5-(*tert*-butoxycarbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C146)**

A reaction mixture of **P2** (2.00 g, 7.30 mmol), *tert*-butyl 6-fluoronicotinate (CAS: 676560-01-3, 1.44 g, 7.30 mmol), and DIEA (2.83 g, 21.9 mmol) in DMF (60 mL) was stirred at 80 °C for 16 h. The reaction mixture was diluted with H_2O (200 mL) and then extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with brine (2 x 100 mL) and then dried with Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo* and then purified by column chromatography (silica gel, 0-25% EtOAc: PE) to provide **C146** (1.80 g, 59.4% yield) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.64 (d, 1H), 7.94 (dd, 1H), 6.94 (d, 1H), 4.79 (s, 2H), 4.59 – 4.47 (m, 1H), 4.31 (q, 2H), 4.08 – 4.00 (m, 2H), 2.85 (t, 2H), 1.53 (s, 9H), 1.39 (d, 6H), 1.34 (t, 3H).

Step 2. Preparation of 6-(3-(ethoxycarbonyl)-1-isopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinic acid **(C147)** and 5-(5-(*tert*-butoxycarbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C148)**

To a solution of **C146** (1.80 mg, 4.34 mmol) in THF (10 mL), MeOH (5 mL) and H_2O (5 mL) was added LiOH (0.456 g, 10.9 mmol) at room temperature and then was stirred at 50 °C for 1 h. The LCMS of the reaction mixture showed 14.7% of **C147** (LC/MS) m/z $(M+H)^+$ = 331.1 and 84.6% of **C148** (LC/MS) m/z $(M+H)^+$ = 387.1 had formed. The reaction mixture was kept in the refrigerator for 48 h and then was concentrated *in vacuo*. The residue was diluted with H_2O (10 mL) and then acidified with 1N HCl to pH~5, which caused a white solid precipitate. The suspension was filtered, and the filter cake was washed with H_2O (2 x 5 mL). The filter cake was collected then concentrated *in vacuo* to provide, according to LCMS, a mixture of 24%

C147 and 76% **C148** (1.60 g, crude) as a white solid. The solid was used directly in the next step without further purification.

C147: (LC/MS) m/z $(M+H)^+$ = 331.2

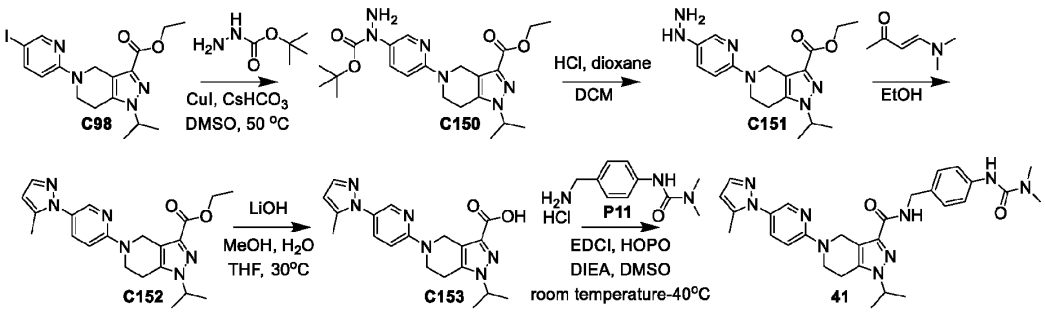
C148 (LC/MS) m/z $(M+H)^+$ = 387.1.

Step 5. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**39**)

At 0 °C, to a solution of **C147** and **C148** (0.500 g, 1.29 mmol) in DMF (10 mL) was added HATU (0.738 g, 1.94 mmol). The reaction mixture was stirred at 0 °C for 20 min then DIEA (0.669 g, 5.18 mmol) and **P11** (0.446 g, 1.94 mmol) were added. After the addition, the reaction mixture was warmed to room temperature and stirred for 16 h. The LCMS of the reaction mixture showed 23.2% of **39** (LC/MS) m/z $(M+H)^+$ = 681.4 and 43.8% of **C149** (LC/MS) m/z $(M+H)^+$ = 562.3 had formed. The suspension was diluted with H_2O (50 mL) and extracted with MeOH: DCM (1:10, 3 x 30 mL). The combined organic layer was washed with brine, dried with Na_2SO_4, and filtered. The filtrate was concentrated *in vacuo* then diluted with DMF (5 mL) and was purified by reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (NH_4OH-NH_4HCO_3), 20 to 60% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 5 min, flow rate= 30 mL/min) and lyophilized to provide **39** (108 mg, 12% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 681.5. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.75 (t, 1H), 8.65 (d, 1H), 8.34 (t, 1H), 8.23 (d, 2H), 8.01 (dd, 1H), 7.41 – 7.35 (m, 4H), 7.20-7.12 (m, 4H), 6.90 (d, 1H), 4.76 (s, 2H), 4.54 – 4.42 (m, 1H), 4.35 (dd, 4H), 3.97 (t, 2H), 2.81 (t, 2H), 1.39 (d, 6H).

Example 41

N-(4-(3,3-Dimethylureido)benzyl)-1-isopropyl-5-(5-(5-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(41)**



Step 1. Preparation of ethyl 5-(5-(1-(*tert*-butoxycarbonyl)hydrazineyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C150)**

Under nitrogen gas, to a reaction mixture of **C98** (0.170 g, 0.386 mmol) in DMSO (1 mL) was added CuI (14.7 mg, 0.0772 mmol) and $CsHCO_3$ (0.377 g, 1.16 mmol) at room temperature. The suspension was stirred at 50 °C for 3 h and filtered through celite. The filtrate was concentrated *in vacuo* and then purified by column chromatography (silica gel, 0-54% THF: PE) to provide **C150** (0.100 g, 58.3% yield) as a yellow oil. (LC/MS) m/z $(M+H)^+$ = 445.2.

Step 2. Preparation of ethyl 5-(5-hydrazineylpyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate hydrochloride **(C151)**

To a reaction mixture of **C150** (0.10 g, 0.22 mmol) in DCM (1 mL) was added HCl in dioxane (8.2 mg, 0.22 mmol) and then stirred at room temperature for 16 h. The suspension was concentrated *in vacuo* to provide **C151** (0.080 g, crude) as a solid. The solid was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.35 (br s, 2H), 7.90 (d, 1H), 7.76 (d, 1H), 7.44 – 7.25 (m, 1H), 6.87 (s, 1H), 4.70 (s, 2H), 4.59 – 4.49 (m, 1H), 4.31 (q, 2H), 3.96 (t, 2H), 2.95 – 2.87 (m, 2H), 1.40 – 1.36 (m, 6H), 1.35 – 1.30 (m, 3H).

Step 3. Preparation of ethyl 1-isopropyl-5-(5-(5-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C152)**

To a reaction mixture of **C151** (0.080 g, 0.21 mmol) in EtOH (1 mL) was added 4-(dimethylamino)but-3-en-2-one (CAS: 1190-91-6, 24 mg, 0.21 mmol) and then stirred at room temperature for 16 h. The suspension was filtered through celite, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-30% EtOAc: PE) to provide **C152** (28 mg, 31% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, 1H), 7.63 – 7.57 (m, 1H), 7.56 (d, 1H), 6.81 (d, 1H), 6.18 (s, 1H), 4.70 (s, 2H), 4.55 – 4.36 (m, 3H), 4.16 – 4.12 (m, 2H), 2.86 (t, 2H), 2.30 (s, 3H), 1.53 (d, 6H), 1.43 (t, 3H).

Step 4. Preparation 1-isopropyl-5-(5-(5-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C153)**

To a solution of **C152** (25 mg, 0.063 mmol) in THF (1.00 mL), H_2O (0.25 mL), and MeOH (0.25 mL) was added LiOH (5.3 mg, 0.13 mmol). The reaction mixture was stirred at 30 °C for 2 h. The suspension's pH was adjusted with citric acid to pH=3 and concentrated *in vacuo* to provide **C153** (23 mg, crude) as a yellow solid. The solid was used directly in the next step without further purification.

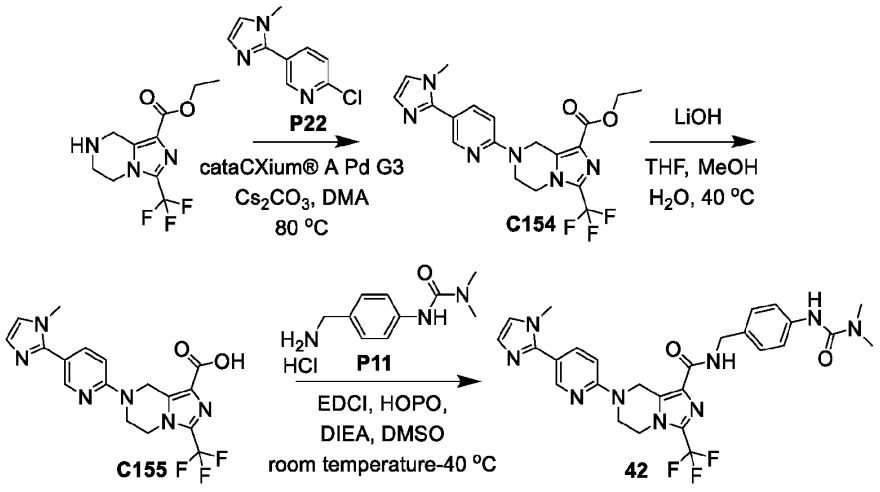
Step 5. Preparation *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(41)**

To a solution of **C153** (25 mg, 0.068 mmol) in DMSO (1 mL) was added HOPO (22 mg, 0.20 mmol), EDCI (31 mg, 0.16 mmol), and DIEA (44 mg, 0.34 mmol). The suspension was stirred at room temperature for 5 min, and then **P11** (23 mg, 0.10 mmol) was added. The

reaction mixture was stirred at 40 °C for 2 h then purified with reverse phase HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 24 to 54% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 3 min, flow rate= 50 mL/min) and lyophilized to provide **41** (26 mg, 71% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 542.4. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, 1H), 7.58 – 7.53 (m, 2H), 7.38 – 7.33 (m, 2H), 7.30 (d, 2H), 7.15 (t, 1H), 6.86 (d, 1H), 6.31 (s, 1H), 6.17 (s, 1H), 4.76 (s, 2H), 4.56 (d, 2H), 4.36 – 4.31 (m, 1H), 4.15 (t, 2H), 3.03 (s, 6H), 2.82 (t, 2H), 2.29 (s, 3H), 1.45 (d, 6H).

Example 42

N-(4-(3,3-Dimethylureido)benzyl)-7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(42)**



Step 1. Preparation of ethyl 7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate (**C154**)

To the reaction mixture of ethyl 5,6,7,8-tetrahydro-3-(trifluoromethyl)imidazo[1,5-*a*]pyrazine-1-carboxylate (CAS: 1598419-92-1; 0.300 g, 1.14 mmol) and **P22** (0.243 g, 1.25 mmol) in DMA (10 mL) was added cataCXium® A Pd G3 (83.0 mg, 0.114 mmol) and Cs_2CO_3 (1.11 g, 3.42 mmol). The suspension was degassed with nitrogen gas and then stirred at 80 °C for 16 h. The reaction mixture was diluted with DCM (3 x 50 mL). The combined organic layer was washed with H_2O (50 mL), then brine (50 mL), and dried with Na_2SO_4. The suspension was concentrated *in vacuo* and then purified by column chromatography (silica gel, 4% MeOH: EtOAc) to provide **C154** (0.258 g, 53.8% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 421.2.

Step 2. Preparation of 7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylic acid (**C155**)

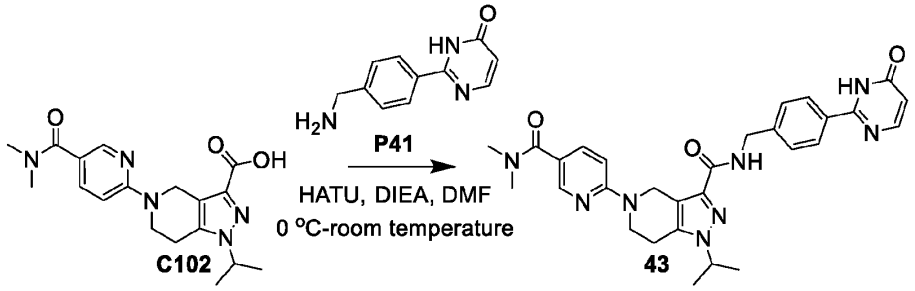
To **C154** (0.258 g, 0.614 mmol) in THF (4.0 mL), H_2O (2.0 mL), and MeOH (1.0 mL) was added LiOH (44.1 mg, 1.84 mmol) at room temperature. The reaction mixture was stirred at 40 °C for 1.5 h and then was concentrated *in vacuo* to remove the organic layer. The resultant aqueous layer was acidified to pH=5-6 with 2N HCl, which caused an off-white solid precipitate. The suspension was filtered, and then the filter cake was washed with H_2O (3 x 10 mL) and dried under high *vacuo*. The filter cake was collected then lyophilized to provide **C155** (0.120 g, 49.8% yield) as a yellow solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.48 (br s, 1H), 8.51 (d, 1H), 7.95 (dd, 1H), 7.24 (s, 1H), 7.10 (d, 1H), 6.97 (s, 1H), 5.12 (s, 2H), 4.31 (t, 2H), 4.14 (t, 2H), 3.73 (s, 3H)

Step 3. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(42)**

To a solution of **C155** (0.050 g, 0.13 mmol) in DMSO (2.0 mL) was added HOPO (42 mg, 0.38 mmol), DIEA (82 mg, 0.64 mmol), and EDCI (59 mg, 0.31 mmol). The reaction mixture was stirred for 10 min at room temperature, and then **P11** (38 mg, 0.17 mmol) was added. The reaction mixture was stirred at 40 °C for 3 h then purified by reverse phase HPLC (Phenomenex Gemini NX C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 22 to 62% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate= 60 mL/min) and lyophilized to provide **42** (0.030 mg, 42% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 568.3. ^{1}H NMR (400 MHz, CD_3OD) δ 8.43 (d, 1H), 7.86 (dd, 1H), 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 2H), 7.16 (d, 1H), 7.07 – 7.00 (m, 2H), 5.15 (s, 2H), 4.49 (s, 2H), 4.34 (t, 2H), 4.21 (t, 2H), 3.74 (s, 3H), 3.00 (s, 6H).

Example 43

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(6-oxo-1,6-dihydropyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(43)**



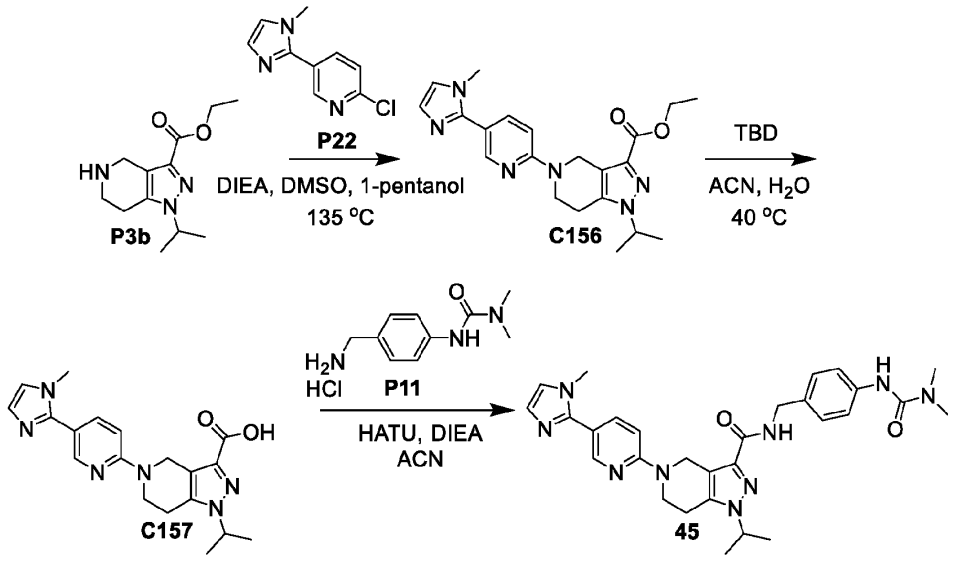
Step 1. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(6-oxo-1,6-dihydropyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(43)**

Under nitrogen gas at 0 °C, to a solution of **C102** (91 mg, 0.38 mmol), **P41** (0.14 g, 0.38 mmol) and HATU (0.15 g, 0.40 mmol) in DMF (1.9 mL) was added DIEA (0.22 g, 1.7 mmol). The reaction mixture was stirred at room temperature for 2 h then purified by reverse phase

HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (0.05% formic acid)/ Mobile Phase B: ACN, 15 to 35% of Mobile Phase B over 11.0 min, 95% of Mobile Phase B hold 2.0 min, flow rate= 35 mL/min) to provide **43** (0.010 g, 4.8% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 541.3. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.57 (t, 1H), 8.23 (d, 1H), 8.09 – 8.02 (m, 3H), 7.63 (dd, 1H), 7.43 (d, 2H), 6.88 (d, 1H), 6.29 (d, 1H), 4.74 (s, 2H), 4.57 – 4.41 (m, 3H), 3.95 (t, 2H), 2.96 (s, 6H), 2.82 (t, 2H), 1.40 (d, 6H).

Example 45

N-(4-(3,3-Dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(45)**



Step 1. Preparation of ethyl 1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate (**C156**)

A reaction mixture of **P3b** (0.100 g, 0.421 mmol), **P22** (97.9 mg, 0.506 mmol), and DIEA (0.218 g, 1.69 mmol) in DMSO (1 mL) and 1-pentanol (1 mL) was heated at 135 °C for 17 h. The solution was diluted with DCM and brine and then concentrated *in vacuo*. The residue was redissolved in DCM and then purified by column chromatography (silica gel, 0-10% MeOH: DCM) to provide **C156** (0.130 g, 78.3% yield) as a yellow oil. (LC/MS) m/z $(M+H)^+$ = 395.3.

Step 2. Preparation of 1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C157**)

To a solution of **C156** (0.050 g, 0.13 mmol) in ACN (1 mL) and H_2O (46 µL) was added TBD (53 mg, 0.38 mmol). The reaction mixture was stirred at 40 °C for 1 h and 20 min, and then NaOH (0.020 g, 0.51 mmol) was added. The suspension was stirred at room temperature for 15 min, and then 12.1M HCl (18 mg, 0.51 mmol) was added. The reaction mixture was

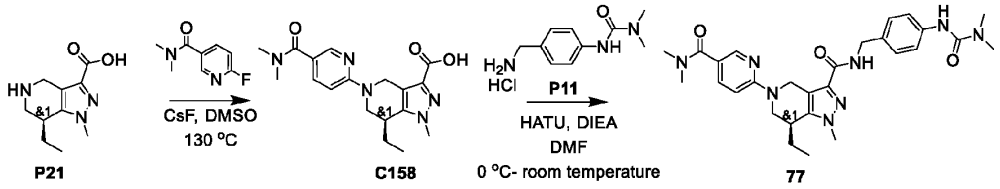
concentrated *in vacuo* to provide **C157** (0.046 g, crude) as a yellow oil. The oil was used directly in the next step without further purification.

Step 3. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(45)**

A reaction mixture of **C157** (46 mg, 0.13 mmol), **P11** (35 mg, 0.15 mmol), DIEA (49 mg, 0.38 mmol), and HATU (48 mg, 0.13 mmol) in ACN (1 mL) was stirred at room temperature for 21 h and then concentrated *in vacuo*. The residue was dissolved in DMSO then acidified with TFA and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 5 to 95% of Mobile Phase B over 9 min, 95% of Mobile Phase B hold 1 min, flow rate= 25 mL/min) and lyophilized to provide **45** (4.3 mg, 6.3% yield). (LC/MS) m/z $(M+H)^+$ = 542.3. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.44 (d, 1H), 8.34 (t, 1H), 8.23 (s, 1H), 7.86 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.24 (br s, 1H), 7.20 – 7.16 (m, 2H), 6.98 (d, 2H), 4.77 (s, 2H), 4.55 – 4.47 (m, 1H), 4.35 (d, 2H), 3.97 (t, 2H), 3.72 (s, 3H) 2.91 (s, 6H), 2.85 (t, 2H), 1.41 (d, 6H).

Example 77

rac-(*R*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(77)**



Step 1. Preparation of *rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C158)**

To a reaction mixture of **P21** (0.186 g, 0.757 mmol) and CsF (0.287 g, 1.89 mmol) in DMSO (3 mL) was added 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 0.127 g, 0.757 mmol). The suspension was stirred at 130 °C for 8 h and then was diluted with H_2O (20 mL). The reaction mixture was cooled to 0 °C, and then aqueous Na_2CO_3 was added to pH= 11 and extracted with EtOAc (2 x 25 mL). The aqueous layer was collected and adjusted to pH=3 with 1M HCl. The acidic aqueous phase was extracted with (1:10, MeOH: DCM, 3 x 20 mL). The combined organic layer was washed with brine (2 x 25 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide **C158** (0.271 g, crude) as a yellow oil. The oil was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.67 (s, 1H), 8.22 (d, 1H), 7.61 (dd, 1H), 6.82 (d, 1H), 4.97 (d, 1H), 4.64 (d, 1H), 4.16 (d, 1H), 3.83 –

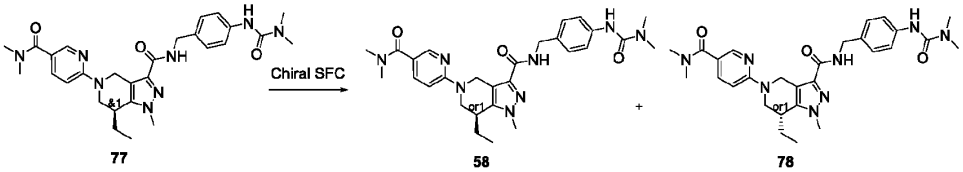
3.74 (m, 3H), 3.19 – 3.12 (m, 1H), 3.00 – 2.90 (m, 7H), 1.62 – 1.51 (m, 1H), 1.46 – 1.33 (m, 1H), 0.99 (t, 3H).

Step 2. Preparation of *rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(77)**

At 0 °C, to a solution of **C158** (0.27 g, 0.68 mmol) in DMF (5 mL) was added HATU (0.28 g, 0.75 mmol). The reaction mixture was stirred at 0 °C for 20 min, and then DIEA (0.35 g, 2.7 mmol) and **P11** (0.16 g, 0.68 mmol) were added at 0 °C. The suspension was stirred at room temperature for 2 h then diluted with H_2O (50 mL) and extracted with (1:10, MeOH: DCM, 3 x 40 mL). The combined organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo* to give a yellow gum. The residue was purified by column chromatography (silica gel; 0-10% MeOH: DCM) to provide **77** (0.32 g, 88% yield) as a yellow solid. (LC/MS) m/z $(M+H)^+$ = 533.4. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.51 (t, 1H), 8.27 – 8.20 (m, 2H), 7.65 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.18 – 7.12 (m, 2H), 6.83 (d, 1H), 5.01 (d, 1H), 4.73 (d, 1H), 4.40 – 4.18 (m, 3H), 3.82 (s, 3H), 3.23 – 3.09 (m, 1H), 3.04 – 2.94 (m, 7H), 2.93 – 2.87 (m, 6H), 1.66 – 1.53 (m, 1H), 1.49 – 1.36 (m, 1H), 1.03 (t, 3H).

Example 58 and 78

rel-(*R* or *S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(58 and 78)**



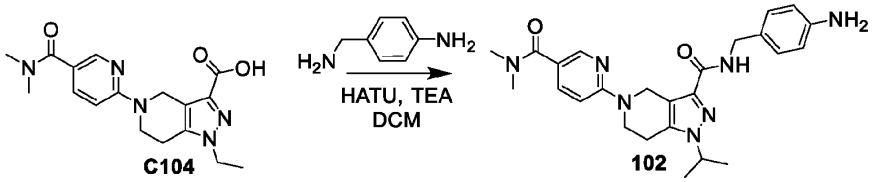
Step 1. Preparation of *rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(58 and 78)**

Example **77** (0.29 g, 0.81 mmol) was separated using chiral SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% MeOH (0.1% NH_4OH); flow rate: 80 mL/ min; gradient time= 45 min] to provide **58** (87 mg, 30% yield) as a white solid and **78** (83 mg, 29% yield) as a white solid. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH with 0.2% of NH_3; isocratic: 40% of Mobile Phase B; flow rate: 3.5 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **58**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 533.41 at retention time: 0.778 min, 100% ee). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (t, 1H), 8.27 – 8.21 (m, 2H), 7.65 (dd, 1H), 7.40 – 7.34 (m, 2H), 7.18 – 7.11 (m, 2H), 6.83 (d, 1H), 5.00 (d, 1H), 4.76 – 4.69 (m, 1H), 4.42 – 4.16 (m, 3H), 3.81 (s, 3H), 3.24

– 3.15 (m, 1H), 3.02 – 2.93 (m, 7H), 2.92 – 2.87 (m, 6H), 1.66 – 1.53 (m, 1H), 1.50 – 1.36 (m, 1H), 1.02 (t, 3H) and Example **78**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 533.41 at retention time: 1.392 min, 100% ee). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.49 (t, 1H), 8.24 – 8.16 (m, 2H), 7.61 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.16 – 7.09 (m, 2H), 6.80 (d, 1H), 4.97 (d, 1H), 4.69 (d, 1H), 4.35 – 4.15 (m, 3H), 3.78 (s, 3H), 3.20 – 3.10 (m, 1H), 2.98 – 2.91 (m, 7H), 2.87 (m, 6H), 1.62 – 1.49 (m, 1H), 1.46 – 1.32 (m, 1H), 0.99 (t, 3H).

Example 102

N-(4-Aminobenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(102)**

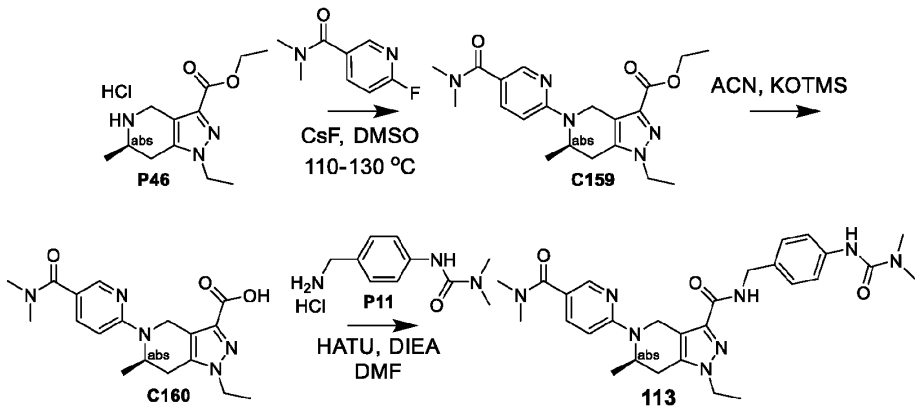


Step 1. Preparation of *N*-(4-aminobenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(102)**

To a reaction mixture of **C104** (1.00 g, 2.80 mmol) in DCM (15 mL) were added 4-aminobenzylamine (CAS: 4403-71-8; 0.431 g, 3.53 mmol), HATU (2.13 g, 5.60 mmol), and TEA (0.581 g, 5.74 mmol). The suspension was stirred at room temperature for 2 h, then diluted with DCM and washed with H_2O. The organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-10% MeOH: DCM) to provide **102** (1.58 g, >95.0% yield) as a yellow foam. (LCMS) *m/z* $(M+H)^+$ = 462.6. ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ 8.24 (d, 1H), 8.11 (t, 1H), 7.64 (dd, 1H), 6.99 (d, 2H), 6.88 (d, 1H), 6.50 (d, 2H), 4.94 (s, 2H), 4.74 (s, 2H), 4.54 – 4.43 (m, 1H), 4.24 (d, 2H), 3.95 (t, 2H), 2.97 (s, 6H), 2.81 (t, 2H), 1.38 (d, 6H).

Example 113

(*R*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(113)**



Step 1. Preparation of ethyl (*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C159)**

To a solution of **P46** (0.380 g, 1.39 mmol) and 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 233 mg, 1.39 mmol) in DMSO (5 mL) was added CsF (527 mg, 3.47 mmol). The reaction mixture was heated at 130 °C for 8 h, and then an additional portion of 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 233 mg, 1.39 mmol) was added. The suspension was heated at 110 °C for 24 h, and then an additional portion of CsF (274 mg, 1.80 mmol) was added. The reaction mixture was stirred at 130 °C for 16 h and then was diluted with H_2O (10 mL). The suspension was extracted with EtOAc (3 x 10 mL). The combined organic layer was washed with brine (2 x 10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, 0-100% EtOAc: PE) to provide **C159** (0.250 g, 46.7% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 386.2. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.30 – 8.27 (m, 1H), 7.68 (dd, 1H), 6.89 (d, 1H), 5.33 – 5.28 (m, 1H), 5.14 (d, 1H), 4.31 (q, 2H), 4.18 – 4.09 (m, 3H), 3.04 – 2.93 (m, 7H), 2.77 (d, 1H), 1.36 – 1.30 (m, 6H), 1.08 (d, 3H).

Step 2. Preparation of (*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C160)**

To a reaction mixture of **C159** (0.250 g, 0.649 mmol) in ACN (5 mL) was added KOTMS (166 mg, 1.30 mmol) at room temperature under nitrogen gas and then stirred for 1 h. The solution was acidified with HCl in dioxane (47.3 mg, 1.30 mmol) to a pH of 5-6, then concentrated *in vacuo* to provide **C160** (232 mg, crude) as a yellow gum. The gum was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 358.1. ^{1}H NMR (600

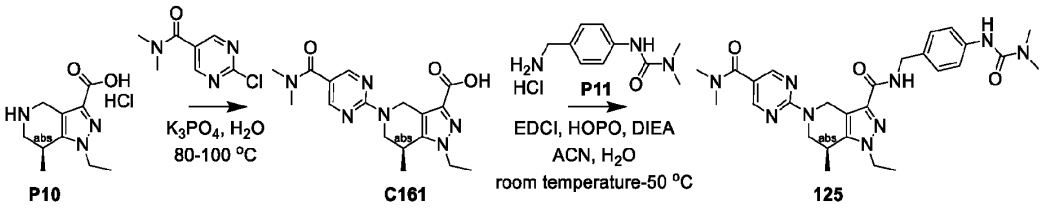
MHz, $(CD_3)_2SO$) δ 8.26 (d, 1H), 7.71 (d, 1H), 6.95 (d, 1H), 5.25 – 5.20 (m, 1H), 5.12 (d, 1H), 4.17 – 4.06 (m, 3H), 2.98 (s, 7H), 2.77 (d, 1H), 1.32 (t, 3H), 1.08 (d, 3H).

Step 3. Preparation of (*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(113)**

To a reaction mixture of **C160** (232 mg, 0.649 mmol) and **P11** (125 mg, 0.649 mmol) in DMF (2.5 mL) were added HATU (271 mg, 0.714 mmol) and DIEA (336 mg, 2.60 mmol). The suspension was stirred at room temperature for 16 h, diluted with H_2O (15 mL), and extracted with EtOAc (3 x 15 mL). The combined organic layer was washed with H_2O (2 x 10 mL), 1M HCl (2 x 10 mL), 1M Na_2CO_3 (2 x 10 mL), and then brine (1x). The organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo* to provide a yellow solid. The solid was purified by reverse phase HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 18 to 58% of Mobile Phase B over 10.0 min, 100% of Mobile Phase B hold 2.5 min, flow rate= 30 mL/min) then lyophilized to provide **113** (134 mg, 38.8% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 533.3. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.26 (d, 1H), 8.23 (s, 1H), 7.65 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.21 – 7.15 (m, 2H), 6.85 (d, 1H), 5.31 – 5.22 (m, 1H), 5.14 (d, 1H), 4.33 (d, 2H), 4.17 – 4.01 (m, 3H), 3.01 – 2.93 (m, 7H), 2.90 (s, 6H), 2.77 – 2.69 (m, 1H), 1.32 (t, 3H), 1.06 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: EtOH with 0.2% of NH_3; isocratic gradient: 40% of Mobile Phase B; backpressure: 1500 psi; flow rate: 3.5 mL/min; column temperature: 35 °C to provide **113**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 533.43 at retention time: 1.503 min, 100% ee).

Example 125

(*S*)-5-(5-(Dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(125)**



Step 1. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid hydrochloride **(C161)**

To a solution of **P10** (6.60 g, 26.9 mmol) and 2-chloro-*N*,*N*-dimethylpyrimidine-5-carboxamide (CAS: 1637587-62-2; 4.98 g, 26.9 mmol) in H_2O (130 mL) was added K_3PO_4 (17.1 g, 80.6 mmol) at room temperature. The reaction mixture was stirred between 80-100 °C for 18 h and then cooled to room temperature. The suspension was extracted MeOH: DCM (100 mL),

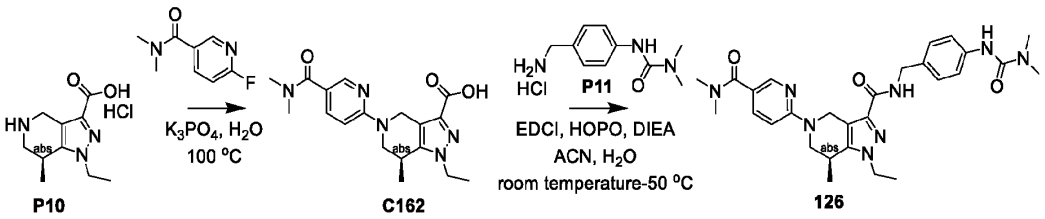
and then the organic layer was discarded. The aqueous layer was acidified to pH<5 with concentrated HCl and then extracted with (1:10) MeOH: DCM (150 mL x3). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to provide **C161** (8.20 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 359.2. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 12.74 (s, 1H), 8.53 (s, 2H), 5.38 (d, 1H), 4.69 (dd, 1H), 4.34 (d, 1H), 4.18 – 4.03 (m, 2H), 3.46 (dd, 1H), 3.28 – 3.19 (m, 1H), 2.99 (br s, 6H), 1.37 (t, 3H), 1.15 (d, 3H). The chiral purity was determined using Chiral HPLC analytical method on Chiralcel OJ-RH 150 mm x 4.6 mm x 5 µm column; Mobile phase A: H_2O (1.5 mL TFA) / Mobile phase B: ACN (1.5 mL TFA);10-80% of Mobile phase B in 8 min then from 80-10% of Mobile phase B in 1 min and held at 10% of Mobile phase B for 6 min; flow rate: 0.8 mL/min; column temperature: 35 °C to provide **C161**: peak 1 (retention time: 7.659 min, 100% ee).

Step 2. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamid **(125)**

To a solution of **C161** (2.70 g, 6.84 mmol), EDCI (1.64 g, 8.55 mmol), and HOPO (0.950 g, 8.55 mmol) in ACN (35 mL) was added DIEA (2.21 g, 17.1 mmol). The solution was stirred at 50 °C for 3.5 h, which caused precipitate to form. The reaction mixture was cooled to room temperature and stirred for 15 min. Then, **P11** (1.65 g, 7.18 mmol), H_2O (0.123 g, 6.84 mmol), and an additional portion of DIEA (3.53 g, 27.3 mmol) were added. The reaction mixture was stirred at 50 °C for 2 h, diluted with EtOAc (50 mL), and washed with H_2O (2 x 50 mL). The aqueous layer was re-extracted with EtOAc (50 mL). The combined organic layer was washed with saturated $NaHCO_3$ (2 x 50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a yellow solid. The yellow solid was purified by column chromatography (silica gel; 0-5% MeOH: DCM) then lyophilized to give **125** (3.39 g, 92.9% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ = 534.3. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (s, 2H), 8.45 (t, 1H), 8.23 (s, 1H), 7.41 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 5.41 (d, 1H), 4.67 (dd, 1H), 4.42 – 4.26 (m, 3H), 4.16 – 4.04 (m, 2H), 3.48 (dd, 1H), 3.28 – 3.19 (m, 1H), 2.99 (br s, 6H), 2.90 (s, 6H), 1.38 (t, 3H), 1.16 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: EtOH with 0.2% of NH_3; gradient: 5-40% of Mobile Phase B in 1.5 min then held at 40% of Mobile phase B for 1.0 min then held at 5% of Mobile phase B for 0.5 min; backpressure: 1500 psi; flow rate: 4.0 mL/min; column temperature: 35 °C to provide **125**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 534.52 at retention time: 1.866 min, 100% ee). $[\alpha]^{20}_D$=-154.134 (c= 8.0 (g/L) in MeOH.

Example 126

(*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(126)**



Step 1. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C162)**

To a solution of 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 3.61 g, 21.5 mmol) and **P10** (5.56 g, 22.6 mmol) in H_2O (110 mL) was added K_3PO_4 (14.4 g, 67.9 mmol) at room temperature. The reaction mixture was stirred at 100 °C for 48 h and then cooled to room temperature. The suspension was extracted with MTBE (20 mL), and then the organic layer was discarded. The aqueous phase was acidified to pH~5-6 with concentrated HCl and then extracted with (1:10) MeOH: DCM (40 mL x3). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to provide **C162** (6.35 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 358.0. ^1H NMR (400 MHz, $CDCl_3$) δ 9.28 (br s, 1H), 8.43 (d, 1H), 7.71 (dd, 1H), 6.77 (d, 1H), 5.01 (d, 1H), 4.46 – 4.34 (m, 2H), 4.22 – 4.04 (m, 2H), 3.49 – 3.40 (m, 1H), 3.15 – 3.04 (m, 7H), 1.47 (t, 3H), 1.29 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: EtOH with 0.2% of NH_3; gradient: 5-40% of Mobile Phase B in 1.5 min then held at 40% of Mobile phase B for 1.0 min then held at 5% of Mobile phase B for 0.5 min; backpressure: 1500 psi; flow rate: 4.0 mL/min; column temperature: 35 °C to provide **C162**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 358.15 at retention time: 1.497 min, 100% ee).

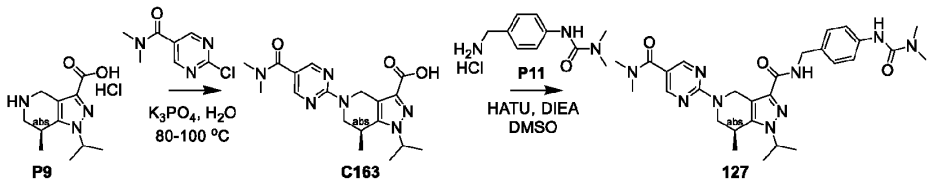
Step 2. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(126)**

To a solution of **C162** (3.00 g, 8.39 mmol), EDCI (2.01 g, 10.5 mmol), and HOPO (1.17 g, 10.5 mmol) in ACN (42 mL) was added DIEA (2.71 g, 21.0 mmol). The solution was stirred at 50 °C for 2 h, which caused precipitate to form. The reaction mixture was cooled to room temperature and stirred for 15 min. Then, P11 (2.02 g, 8.81 mmol), H_2O (0.151 g, 8.39 mmol), and an additional portion of DIEA (4.34 g, 33.6 mmol) were added. The reaction mixture was stirred at 50 °C for 4 h, diluted with EtOAc (30 mL), and washed with H_2O (2 x 30 mL). The aqueous layer was re-extracted with EtOAc (10 mL). The combined organic layer was washed with saturated $NaHCO_3$ (2 x 30 mL) and brine (30 mL). The organic layer was dried over

Na_2SO_4, filtered, and concentrated *in vacuo* to give a yellow solid. The solid was purified by column chromatography (silica gel; 0-10% MeOH: DCM) and then lyophilized to give **126** (2.20 g, 49.2% yield) as a yellow solid. (LCMS) *m/z* $(M+H)^+$ = 533.4. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.25 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 6.89 (d, 1H), 5.05 (d, 1H), 4.41 – 4.25 (m, 4H), 4.17 – 4.04 (m, 2H), 3.43 – 3.36 (m, 1H), 3.26 – 3.17 (m, 1H), 2.98 (br s, 6H), 2.90 (s, 6H), 1.38 (t, 3H), 1.20 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2 / Mobile phase B: EtOH with 0.2% of NH_3; Isocratic: 40% Mobile phase B; backpressure: 1500 psi; flow rate: 3.5 mL/min; column temperature: 35 °C to provide **126**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 533.61 at retention time: 1.530 min, 100% ee). $[\alpha]^{20}_D$=-121.791 (c= 5.5 (g/L) in MeOH.

Example 127

(*S*)-5-(5-Dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(127)**



Step 1. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C163)**

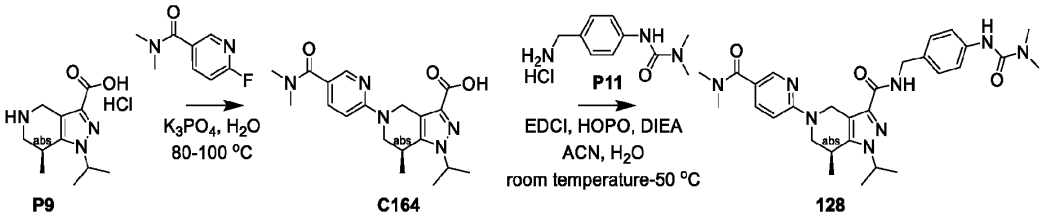
To a solution of 2-chloro-*N,N*-dimethylpyrimidine-5-carboxamide (CAS: 1637587-62-2; 3.86 g, 20.8 mmol) and **P9** (5.40 g, 20.8 mmol) in H_2O (108 mL) was added K_3PO_4 (13.2 g, 62.4 mmol) at room temperature. The reaction mixture was heated between 80-100 °C for 18 h and then cooled to room temperature. The reaction mixture was extracted with EtOAc (50 mL x2), and the combined organic layer was discarded. The aqueous layer was acidified to pH=5-6 with aqueous HCl and then extracted with (1:10) MeOH: DCM (50 mL x4). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give **C163** (7.10 g, crude) as a light yellow solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 373.2. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 12.73 (br s, 1H), 8.53 (s, 2H), 5.43 (d, 1H), 4.80 – 4.73 (m, 1H), 4.61 – 4.44 (m, 1H), 4.28 (d, 1H), 3.44 – 3.37 (m, 1H), 3.29 – 3.18 (m, 1H), 2.99 (br s, 6H), 1.40 (dd, 6H), 1.17 – 1.11 (m, 3H). The chiral purity was determined using SFC analytical method on Chiralpak AD-3 100 mm x 4.6 mm x 3 µm; Mobile phase A: CO_2/ Mobile phase B: 40% EtOH with 0.2% of NH_3; backpressure: 1500 psi; flow rate: 2.8 mL/min; column temperature: 35 °C to provide **C163**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 373.19 at retention time: 1.096 min, 100% ee).

Step 2. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(127)**

To a solution of **C163** (0.060 g, 0.16 mmol) in DMSO (1 mL) was added DIEA (0.062 g, 0.48 mmol), **P11** (0.041 g, 0.18 mmol), and HATU (0.092 g, 0.24 mmol). The reaction was stirred at room temperature for 10 min and then was filtered. The filtrate was purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/ Mobile Phase B: ACN, 15 to 95% of Mobile Phase B over 9.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide **127** (15 mg, 17% yield) as a solid. (LCMS) *m/z* $(M+H)^+$ = 548.9. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (s, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 5.47 (d, 1H), 4.75 (dd, 1H), 4.58 – 4.46 (m, 1H), 4.40 – 4.29 (m, 3H), 3.42 (dd, 1H), 3.29 – 3.23 (m, 1H) 3.04 - 2.94 (m, 6H), 2.91 (s, 6H), 1.38 (dd, 6H), 1.11 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm; Mobile phase A: CO_2/ Mobile phase B: isopropyl alcohol with 0.2% NH_3; Isocratic: 40% Mobile phase B; backpressure: 1500 psi; flow rate: 3.5 mL/min; column temperature: 35 °C to provide **127**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 548.70 at retention time: 1.882 min, 100% ee). $[\alpha]^{20}_D$=-149.239 (c= 1.5 (g/L) in MeOH).

Example 128

(*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(128)**



Step 1. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C164)**

To a solution of 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 2.91 g, 17.3 mmol) and **P9** (5.00 g, 19.2 mmol) in H_2O (100 mL) was added K_3PO_4 (12.3 g, 57.7 mmol) at room temperature. The reaction mixture was stirred between 80-100 °C for 18 h and then cooled to room temperature. To the suspension was added another portion of 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 0.227 g, 1.35 mmol), then the reaction mixture was stirred between 80-100 °C for 48 h. The suspension was cooled to room temperature and extracted with EtOAc (100 mL x 4). The combined organic layer was discarded. The aqueous layer was acidified to pH=5-6 with aqueous HCl then extracted with (1:10) MeOH: DCM (50 mL x9). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give **C164** (5.80 g, crude) as a light yellow solid. The solid was used directly in the next step without

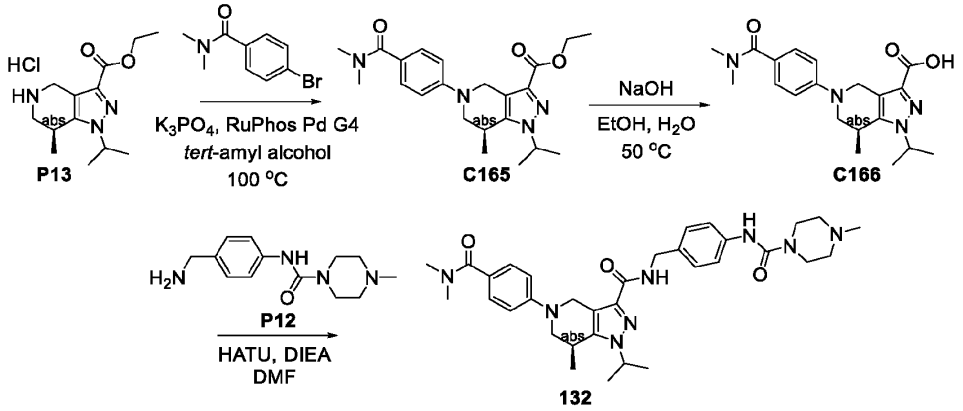
further purification. (LCMS) *m/z* $(M+H)^+$ = 372.1. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.70 (br s, 1H), 8.26 – 8.24 (m, 1H), 7.64 (dd, 1H), 6.91 (d, 1H), 5.08 (d, 1H), 4.60 – 4.49 (m, 1H), 4.43 – 4.36 (m, 1H), 4.19 (d, 1H), 3.37 - 3.35 (m, 1H), 3.26 – 3.21 (m, 1H), 2.98 (s, 6H), 1.40 (dd, 6H), 1.20 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak AD-3 100 mm x 4.6 mm x 3 µm; Mobile phase A: CO_2 / Mobile phase B: 40% EtOH with 0.2% of NH_3; backpressure: 1500 psi; flow rate: 2.8 mL/min; column temperature: 35 °C to provide **C164**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 372.17 at retention time: 1.254 min, 100% ee).

Step 2. Preparation of (*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(128)**

To a solution of **C164** (3.20 g, 8.61 mmol), EDCI (2.06 g, 10.8 mmol), and HOPO (1.20 g, 10.8 mmol) in ACN (50 mL) was added DIEA (4.45 g, 34.4 mmol). The solution was stirred at 50 °C for 2 h, which caused precipitate to form. The reaction mixture was cooled to room temperature, then **P11** (2.18 g, 9.47 mmol), H_2O (0.155 g, 8.61 mmol), and an additional portion of DIEA (4.45 g, 34.4 mmol) were added. The reaction mixture was stirred at 50 °C for 6 h and then diluted with H_2O (20 mL). The suspension was concentrated *in vacuo* to remove the solvent and leave the aqueous layer. The aqueous layer was extracted with (1:10) MeOH: DCM (3 x 70 mL). The combined organic layer was washed with saturated $NaHCO_3$ (15 mL) and brine (15 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a yellow solid. The yellow solid was purified by column chromatography (silica gel; 0-10% MeOH: DCM) and then lyophilized to give **128** (1.75 g, 37.2% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ = 547.3. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.18 – 8.16 (m, 2H), 7.57 (dd, 1H), 7.34 – 7.29 (m, 2H), 7.14 – 7.08 (m, 2H), 6.82 (d, 1H), 5.03 (d, 1H), 4.50 – 4.41 (m, 1H), 4.39 – 4.23 (m, 3H), 4.17 (d, 1H), 3.36 – 3.35 (m, 1H), 3.18 – 3.12 (m, 1H), 2.91 (s, 6H), 2.84 (s, 6H), 1.35 (dd, 6H), 1.13 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm; Mobile phase A: CO_2 / Mobile phase B: EtOH with 0.2% NH_3; Isocratic 40% of Mobile phase B; backpressure: 1500 psi; flow rate: 4.0 mL/min; column temperature: 35 °C to provide **128**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 547.54 at retention time: 1.035 min, 99% ee). $[\alpha]^{25}_D$=-12.573 (c= 2.6 (g/L) in MeOH).

Example 132

(*S*)-5-(4-(Dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(132)**



Step 1. Preparation of ethyl (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C165)**

A reaction mixture of 4-bromo-*N,N*-dimethylbenzamide (0.344 g, 1.51 mmol), K_3PO_4 (0.667 g, 3.14 mmol) and RuPhos Pd G4 (0.107 g, 0.126 mmol) was degassed with nitrogen gas before a solution of **P13** (0.362 g, 1.26 mmol) in *tert*-amyl alcohol (3 mL) was added. The suspension was stirred at 100 °C for 25 h, then filtered and concentrated *in vacuo*. The residue was dissolved in DCM and purified by column chromatography (silica gel, 20-100% EtOAc: heptane) to provide **C165** (0.512 g, crude) as a yellow oil. The oil was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 399.6. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 7.38 – 7.34 (m, 2H), 7.03 – 6.98 (m, 2H), 4.64 – 4.56 (m, 1H), 4.53 (d, 1H), 4.31 (q, 2H), 4.11 (d, 1H), 3.88 – 3.83 (m, 1H), 3.32 – 3.22 (m, 2H), 2.98 (s, 6H), 1.43 (dd, 6H), 1.34 (t, 3H), 1.31 (d, 3H).

Step 2. Preparation of (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C166)**

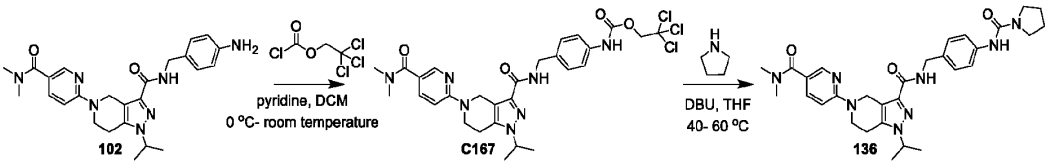
To a solution of **C165** (0.500 g, 1.25 mmol) in EtOH (3 mL) was added NaOH (0.151 g, 3.76 mmol) and H_2O (1 mL). The reaction mixture was stirred at 50 °C for 25 h, then acidified with HCl and concentrated *in vacuo* to provide **C166** (0.465 g, crude) as a yellow solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 371.4. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 7.37 – 7.31 (m, 2H), 7.01 – 6.95 (m, 2H), 4.61 – 4.52 (m, 1H), 4.50 (d, 1H), 4.11 – 4.05 (m, 1H), 3.82 (dd, 1H), 3.29 (dd, 1H), 3.24 – 3.18 (m, 1H), 2.96 (s, 6H), 1.44 – 1.39 (m, 6H), 1.29 (d, 3H).

Step 3. Preparation of (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(132)**

To a solution of **C166** (37 mg, 0.10 mmol) and **P12** (32 mg, 0.10 mmol) in DMF (1 mL) was added HATU (38 mg, 0.10 mmol). The suspension was stirred at room temperature for 2 min, and then DIEA (64 mg, 0.50 mmol) was added. The yellow solution was stirred at room temperature for 2 h, then diluted with MeOH and purified by reverse phase HPLC (Phenomenex Gemini NX C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/ Mobile Phase B: ACN, 26- 66% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold for 2 min, flow rate: 60 mL/min) and lyophilized to provide **132** (0.020 g, 34% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ = 601.3. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (s, 1H), 8.36 (t, 1H), 7.40 – 7.28 (m, 4H), 7.21 – 7.12 (m, 2H), 7.00 – 6.91 (m, 2H), 4.59 – 4.48 (m, 2H), 4.36 – 4.30 (m, 2H), 4.10 (d, 1H), 3.85 – 3.77 (m, 1H), 3.41 (t, 4H), 3.28 – 3.16 (m, 2H), 2.97 – 2.91 (m, 6H), 2.29 (t, 4H), 2.18 (s, 3H), 1.47 – 1.37 (m, 6H), 1.28 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: EtOH (0.2% NH_3); 5 to 40% of Mobile phase B in 1.5 min and held at 40% of Mobile phase B for 1.0 min then 5% of Mobile phase B for 0.5 min; backpressure: 1500 psi; flow rate: 4.0 mL/min; column temperature: 35 °C to provide peak 1: ((SFC-MS) *m/z* $(M+H)^+$ = 601.32 at retention time: 1.830 min, 0.27% ee) and **132**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 601.31 at retention time: 2.105 min, 99.73% ee).

Example 136

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**136**)



Step 1. Preparation of 2,2,2-trichloroethyl (4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate **(C167)**

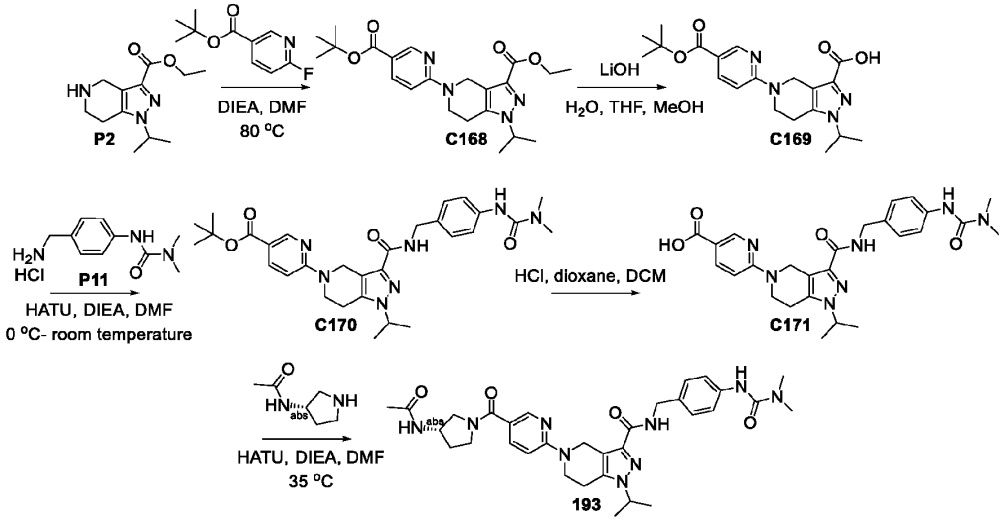
At 0 °C, to a solution of **102** (1.3 g, 2.8 mmol) in DCM (13 mL) was added pyridine (0.49 g, 6.2 mmol) followed by a solution of 2,2,2-trichloroethoxycarbonylchloride (0.77 g, 3.6 mmol) in DCM (1 mL) dropwise. The reaction mixture was stirred for 30 min at 0 °C, then warmed to room temperature and concentrated *in vacuo*. The residue was dissolved in MeOH: DCM then purified by column chromatography (silica gel, 0-10% MeOH: DCM) to provide **C167** (1.7 g, 93% yield) as a white foam. (LCMS) *m/z* $(M+H)^+$ = 638.6.

Step 2. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide (**136**)

In a gold para-dox® plate was added a reaction mixture of pyrrolidine (0.070 mL) and DBU (0.030 mL) in THF (0.25 mL) and then shaken at 40 °C for 2 h. A solution of **C167** (6.4 mg, 0.010 mmol) in THF (0.023 mL) was added to the suspension, and then the reaction mixture was sealed and shaken at 60 °C overnight. The suspension was dissolved in (1:1, MeOH: DCE, 0.35 mL) and then filtered. The filter cake was rinsed with (1:1, MeOH: DCE, 0.35 mL x 2). The filtrate was concentrated *in vacuo* and then dissolved in (1:1, MeOH: DCE, 0.20 mL) and shaken at room temperature for 2h. The solution was purified by reverse phase HPLC (C_{18} 50 mm x 10 mm x 5 µm column; Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 5 to 95% of Mobile Phase B over 5 min, flow rate: 4.0 mL/min) to provide **136** (1.1 mg, 20% yield). (LCMS) *m/z* $(M+H)^+$ = 559.4.

Example 193

(*S*)-5-(5-(3-Acetamidopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(193)**



Step 1. Preparation of ethyl 5-(5-(tert-butoxycarbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C168)**

A suspension of **P2** (1.85 g, 6.76 mmol) in DMF (40 mL) was added DIEA (2.62 g, 20.3 mmol) and *tert*-butyl 6-fluoronicotinate (CAS: 676560-01-3, 1.33 g, 6.76 mmol). The reaction mixture was stirred at 80 °C for 16 h, and then an additional portion of *tert*-butyl 6-fluoronicotinate (CAS: 676560-01-3,133 mg, 0.676 mmol) was added. The reaction mixture was stirred at 80 °C for 4 h and then was diluted with H_2O (300 mL). The suspension was extracted with EtOAc (3 x 100 mL). The combined organic layer was washed with brine (2 x 100 mL), dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-25% EtOAc: PE) to provide **C168** (1.86 g, 66.4%) as a white solid.

Step 2. Preparation of 5-(5-(*tert*-butoxycarbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid (**C169**)

The same reaction was conducted in two batches and then combined for acidification. To a solution of **C168** (1.76 g, 4.25 mmol) in THF (10 mL), MeOH (5 mL) and H_2O (10 mL) was added LiOH (0.445 g, 10.6 mmol) to form the first batch then stirred for 16 h.

A second batch of the same reaction was conducted with **C168** (0.100 g, 0.241 mmol). The two batches were combined and then concentrated *in vacuo*. The residue was diluted with H_2O (15 mL) and acidified with 1M HCl to pH~4-5, which caused precipitate to form. The suspension was filtered, and the filter cake was washed with H_2O (2 x 10 mL). The filter cake was collected and dried by high vacuum to provide **C169** (1.73 g, crude) as an off-white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 387.1.

Step 3. Preparation of *tert*-butyl 6-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinate **(C170)**

At 0 °C, to a solution of **C169** (1.73 g, 4.49 mmol) in DMF (30 mL) was added HATU (1.88 g, 4.94 mmol) and stirred for 20 min; then, DIEA (2.32 g, 17.9 mmol) and **P11** (1.13 g, 4.94 mmol) were added. The reaction mixture was stirred at room temperature for 16 h and then diluted with H_2O (200 mL). The suspension was extracted with (1:10, MeOH: DCM, 3 x 100 mL). The combined organic layer was washed with brine (2 x 150 mL), dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-5% MeOH: DCM) to provide impure **C170** (4.00 g), which was re-purified again by column chromatography (silica gel, 0-2.5% MeOH: DCM) to provide **C170** (3.5 g, >95.0% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ = 562.2. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (d, 1H), 8.35 (t, 1H), 8.26 – 8.21 (m, 1H), 7.92 (dd, 1H), 7.44 – 7.36 (m, 2H), 7.21 – 7.14 (m, 2H), 6.91 (d, 1H), 4.80 (s, 2H), 4.54 – 4.43 (m, 1H), 4.35 (d, 2H), 4.04 – 3.94 (m, 2H), 2.96 – 2.89 (m, 6H), 2.86 – 2.79 (m, 2H), 1.52 (s, 9H), 1.40 (d, 6H).

Step 4. Preparation of 6-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinic acid **(C171)**

To a solution of **C170** (3.50 g, 6.23 mmol) in DCM (70 mL) was added 2M HCl in dioxane (35 mL) and then stirred for 16 h, and an additional portion of 2M HCl in dioxane (30 mL) was added. The reaction mixture was stirred for 2h and then was diluted with H_2O (20 mL) and concentrated *in vacuo* to remove the organic layer. The aqueous layer was basified with $NaHCO_3$ until pH=5, which caused white precipitation to form. The mixture was filtered, and then the filter cake was washed with H_2O (2 x 30 mL), dried under a high vacuum, and then lyophilized to provide **C171** (2.22 g, 69.8% yield) as a white solid (LCMS) *m/z* $(M+H)^+$ = 506.4.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.51 (s, 1H), 8.65 (d, 1H), 8.35 (t, 1H), 8.23 (s, 1H), 7.96 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 6.91 (d, 1H), 4.80 (s, 2H), 4.58 – 4.43 (m, 1H), 4.34 (d, 2H), 4.04 – 3.97 (m, 2H), 2.91 (s, 6H), 2.86 – 2.80 (m, 2H), 1.39 (d, 6H).

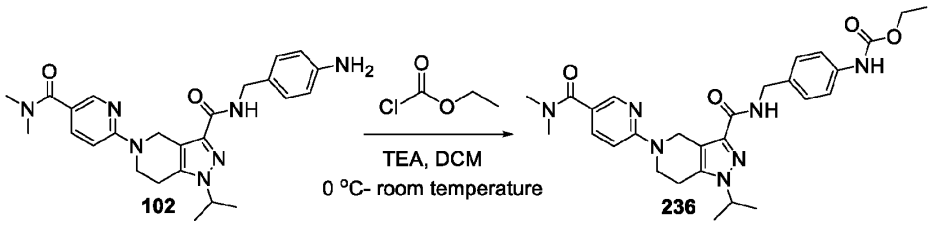
Step 5. Preparation of (*S*)-5-(5-(3-acetamidopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(193)**

A solution of (*S*)-*N*-(pyrrolidin-3-yl)acetamide (CAS: 114636-31-6; 1.9 mg, 15 μmol) in (1:9, DIEA: DMF, 5.0 μL: 45 μL) was shaken at 30 °C for 1.5 h.

In a gold para-dox® plate, a solution of **C171** (66 mg, 0.13 mmol), HATU (74 mg, 0.19 mmol), and DIEA (0.065 mL) in DMF (0.58 mL) was stirred for 20 min and then shaken at 35 °C for 19 h. The solution was concentrated under nitrogen gas. The residue was dissolved in (1:1, MeOH: DCE) and then shaken at 30 °C for 10 min. The suspension was filtered, and then the filter cake was rinsed with (1:1, MeOH: DCE, 0.60 mL). The filtrate was concentrated with nitrogen gas. The residue was dissolved in DMSO (0.15 mL) and then shaken at 30 °C for 30 min. TFA (2.0 μL) and H_2O (0.50 mL) were added to the suspension. The suspension was concentrated with nitrogen gas then dissolved in DMSO (0.15 mL) and purified by reverse phase HPLC (C_{18} 50 mm x 10 mm x 5 μm column; Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% formic acid), 50 to 80% of Mobile Phase B over 5 min, flow rate: 4.0 mL/min) to provide **193** (2.1 mg, 34% yield). (LCMS) *m/z* $(M+H)^+$ = 616.4.

Example 236

Ethyl (4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate **(236)**

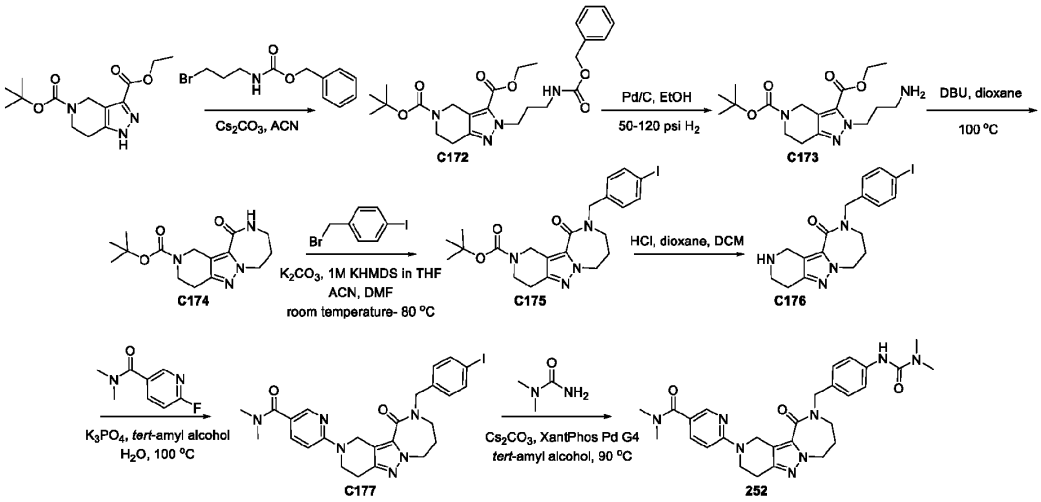


Step 1. Preparation of ethyl (4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate **(236)** At 0 °C, to a reaction mixture of **102** (0.200 g, 0.433 mmol) in DCM (2 mL) was added TEA (0.132 g, 1.30 mmol), then a solution of ethyl carbonochloridate (CAS: 541-41-3; 0.310 g, 2.86 mmol) in DCM (1 mL) dropwise. The reaction mixture was sealed and stirred at room temperature for 16 h. The suspension was diluted with H_2O (10 mL) and stirred at 0 °C for 30 min, and then the mixture's pH was adjusted to pH=8. The reaction mixture was extracted with DCM (2 x 10 mL). The organic layers were combined, dried with Na_2SO_4, and concentrated *in vacuo*. The residue

was purified by reverse phase HPLC (Welch Xtimate C_{18} 150 mm x 25 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/Mobile Phase B: ACN, 38 to 58% of Mobile Phase B over 11 min, 100% of Mobile Phase B hold 2 min, flow rate: 60 mL/min) and lyophilized to provide **236** (84.0 mg, 36.4% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ =534.3. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 9.46 (s, 1H), 8.28 (t, 1H), 8.16 – 8.14 (m, 1H), 7.55 (dd, 1H), 7.30 (d, 2H), 7.14 (d, 2H), 6.80 (d, 1H), 4.66 (s, 2H), 4.46 – 4.36 (m, 1H), 4.27 (d, 2H), 4.02 (q, 2H), 3.86 (t, 2H), 2.88 (s, 6H), 2.73 (t, 2H), 1.31 (d, 6H), 1.14 (t, 3H).

Example 252

6-(10-(4-(3,3-Dimethylureido)benzyl)-11-oxo-1,3,4,7,8,9,10,11-octahydro-2*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepin-2-yl)-*N*,*N*-dimethylnicotinamide (**252**)



Step 1. Preparation of 5-(*tert*-butyl) 3-ethyl 2-(3-(((benzyloxy)carbonyl)amino)propyl)-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C172**)

A reaction mixture of 5-(*tert*-butyl) 3-ethyl 1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (CAS: 518990-23-3; 1.00 g, 3.39 mmol), benzyl (3-bromopropyl)carbamate (CAS: 39945-54-5; 967 mg, 3.56 mmol) and Cs_2CO_3 (1.65 g, 5.08 mmol) in ACN (20 mL) was stirred at room temperature for ~72 h. The reaction mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in DCM and then purified by column chromatography (silica gel, 0-60% EtOAc: heptane) to provide **C172** (1.02 g, 61.9% yield) as a clear oil. (LCMS) *m/z* $(M+H)^+$ =487.3. ^1H NMR (600 MHz, $(CD_3)_2SO$) δ 7.41 – 7.26 (m, 6H), 5.01 (s, 2H), 4.53 (s, 2H), 4.45 (t, 2H), 4.32 – 4.28 (m, 2H), 3.60 (t, 2H), 3.01 (q, 2H), 2.64 (t, 2H), 1.93 – 1.85 (m, 2H), 1.44 – 1.41 (m, 9H), 1.32 (t, 3H).

Step 2. Preparation of 5-(*tert*-butyl) 3-ethyl 2-(3-aminopropyl)-2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxylate (**C173**)

Pd/C (10 wt%, 0.153 g, 1.44 mmol) and **C172** (1.00 g, 2.06 mmol) were added to a pressure vessel in EtOH (10 mL). The reaction mixture was stirred at 50 psi of H_2 gas for ~24 h. An additional portion of Pd/C (10 wt%, 0.153 g, 1.44 mmol) was added and stirred at 120 psi of H_2 gas for ~24 h. The reaction mixture was filtered through celite, and then the filtrate was concentrated *in vacuo* to provide **C173** (0.745 g, crude) as a clear oil. The oil was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 4.55 – 4.41 (m, 3H), 4.37 – 4.26 (m, 3H), 3.60 (t, 2H), 3.50 – 3.40 (m, 2H), 2.64 (t, 2H), 2.57 – 2.52 (m, 2H), 1.92 – 1.77 (m, 2H), 1.44 – 1.41 (m, 9H), 1.33 (t, 3H).

Step 3. Preparation of *tert*-butyl 11-oxo-1,3,4,7,8,9,10,11-octahydro-2*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepine-2-carboxylate **(C174)**

To a solution of **C173** (0.724 g, 2.05 mmol) in dioxane (10 mL) was added DBU (0.109 g, 0.719 mmol) and then stirred at 100 °C for 23 h. The reaction mixture was concentrated *in vacuo* to provide **C174** (0.820 g, crude) as a yellow oil. The oil was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.89 (s, 1H), 4.24 – 4.20 (m, 2H), 4.09 (t, 2H), 3.03 – 2.87 (m, 4H), 2.42 – 2.33 (m, 2H),1.91 – 1.83 (m, 2H), 1.19 – 1.13 (m, 9H).

Step 4. Preparation of *tert*-butyl 10-(4-iodobenzyl)-11-oxo-1,3,4,7,8,9,10,11-octahydro-2*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepine-2-carboxylate **(C175)**

To a solution of **C174** (0.629 g, 2.05 mmol) in ACN (10 mL) was added 1-(bromomethyl)-4-iodobenzene (CAS: 589-87-7; 0.610 g, 2.05 mmol) and K_2CO_3 (426 mg, 3.08 mmol). The reaction mixture was stirred at 80 °C for 2 h and dissolved in THF (10 mL). The solution was treated with 1M KHMDS in THF (2.0 mL) at room temperature and then diluted with DMF (1 mL). The reaction mixture was stirred at room temperature for 2.5 h and then concentrated *in vacuo*. The residue was suspended with H_2O and extracted with EtOAc. The organic layer was concentrated *in vacuo,* and then the residue was dissolved in DCM. The suspension was purified by column chromatography (silica gel, 0-80% EtOAc: heptane) to provide **C175** (0.496 g, 46.3% yield) as a white foam. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.76 – 7.64 (m, 2H), 7.22 – 7.13 (m, 2H), 4.62 (s, 2H), 4.47 (s, 2H), 4.26 (t, 2H), 3.60 (t, 2H), 3.39 – 3.34 (m, 2H), 2.62 (t, 2H), 2.07 – 1.98 (m, 2H), 1.42 (s, 9H).

Step 5. Preparation of 10-(4-iodobenzyl)-1,2,3,4,7,8,9,10-octahydro-11*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepin-11-one hydrochloride **(C176)**

To a solution of **C175** (0.496 g, 0.949 mmol) in DCM (10 mL) was added 4M HCl in dioxane (0.95 mL). The reaction mixture was concentrated *in vacuo* to provide **C176** (0.436 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ =423.3. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.12 (s, 1H), 7.75 – 7.69 (m, 2H),

7.21 – 7.14 (m, 2H), 4.65 – 4.60 (m, 2H), 4.35 – 4.29 (m, 2H), 4.27 – 4.21 (m, 2H), 3.43 – 3.34 (m, 4H), 2.91 – 2.83 (m, 2H), 2.12 – 2.01 (m, 2H).

Step 6. Preparation of 6-(10-(4-iodobenzyl)-11-oxo-1,3,4,7,8,9,10,11-octahydro-2*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepin-2-yl)-*N,N*-dimethylnicotinamide **(C177)**

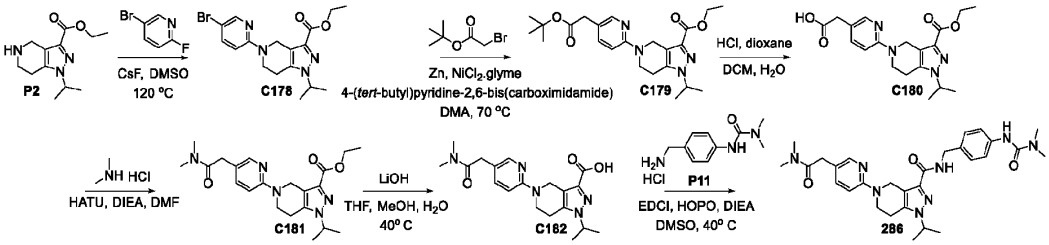
To a mixture of **C176** (0.436 g, 0.950 mmol), K_3PO_4 (0.605 g, 2.85 mmol), H_2O (4 mL), and *tert*-amyl alcohol (4 mL), 6-fluoro-*N,N*-dimethylnicotinamide (CAS: 1032251-82-3; 176 mg, 1.05 mmol) was added. The reaction mixture was stirred at 100 °C for ~72 h, diluted with H_2O, and extracted with EtOAc. The organic layer was washed with H_2O and concentrated *in vacuo* to provide **C177** (0.632 g, crude) as a yellow oil. The oil was used directly in the next step without further purification.

Step 7. Preparation of 6-(10-(4-(3,3-dimethylureido)benzyl)-11-oxo-1,3,4,7,8,9,10,11-octahydro-2*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepin-2-yl)-*N,N*-dimethylnicotinamide (**252**)

A reaction mixture of **C177** (0.080 g, 0.14 mmol), 1,1-dimethylurea (CAS: 598-94-7; 37 mg, 0.42 mmol), Cs_2CO_3 (0.14 g, 0.42 mmol) and XantPhos Pd G4 (13 mg, 0.014 mmol) was degassed with nitrogen gas then *tert*-amyl alcohol (1 mL) was added. The suspension was stirred at 90 °C for 2 h and then filtered, and the filtrate was concentrated *in vacuo*. The residue was suspended in DMSO, filtered and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 5 to 95% of Mobile Phase B over 10 min, flow rate: 25 mL/min) to provide **252** (4.6 mg, 6.2% yield). (LC/MS) m/z $(M+H)^+$ = 531.4. ^1H NMR (600 MHz, $(CD_3)_2SO$) δ 8.28 (s, 1H), 8.24 (d, 1H), 7.64 (dd, 1H), 7.48 – 7.44 (m, 2H), 7.27 – 7.23 (m, 2H), 6.92 (d, 1H), 4.74 (s, 2H), 4.60 (s, 2H), 4.24 (t, 2H), 3.94 (t, 2H), 3.33 (t, 2H), 2.97 (s, 6H), 2.92 (s, 6H), 2.73 (t, 2H), 1.99 – 1.92 (m, 2H).

Example 286

5-(5-(2-(Dimethylamino)-2-oxoethyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(286)**



Step 1. Preparation of ethyl 5-(5-bromopyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C178)**

To a solution of **P2** (4.10 g, 15.0 mmol) and CsF (5.69 g, 37.4 mmol) in DMSO (50 mL) was added 5-bromo-2-fluoropyridine (CAS: 766-11-0; 2.64 g, 15.0 mmol). The reaction mixture

was stirred at 120 °C for 5 h. The solution was diluted with H_2O (40 mL) and extracted with EtOAc (3 x 50 mL). The organic layer was washed with brine (50 mL), dried with Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-25% EtOAc: PE) to provide **C178** (3.20 g, 54.3% yield) as a yellow solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.18 (d, 1H), 7.70 (dd, 1H), 6.90 (d, 1H), 4.64 (s, 2H), 4.56 – 4.45 (m, 1H), 4.28 (q, 2H), 3.87 (t, 2H), 2.80 (t, 2H), 1.36 (d, 6H), 1.30 (t, 3H).

Step 2. Preparation of ethyl 5-(5-(2-(*tert*-butoxy)-2-oxoethyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C179)**

Under nitrogen gas, to **C178** (0.58 g, 1.5 mmol) was added *tert*-butyl bromoacetate (CAS: 1211526-62-3; 0.29 g, 1.5 mmol), Zn (0.27 g, 3.7 mmol), $NiCl_2$.glyme (32 mg, 0.15 mmol), 4-(*tert*-butyl)pyridine-2,6-*bis*(carboximidamide) (CAS: 3003061-14-8; 43 mg, 0.15 mmol) and DMA (10 mL). The solution was degassed with nitrogen gas for 2 min and then stirred at 70 °C for 16 h. The reaction mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was diluted with EtOAc (20 mL) and then washed with H_2O (3 x 10 mL) followed by brine (2 x 10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-30% EtOAc: PE) to provide **C179** (87 mg, 14% yield) as a colorless oil. (LC/MS) m/z $(M+H)^+$ = 429.2.

Step 3. Preparation of 2-(6-(3-(ethoxycarbonyl)-1-isopropyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyridin-3-yl)acetic acid **(C180)**

To a solution of **C179** (87 mg, 0.20 mmol) in DCM (3.0 mL), 2M HCl in dioxane (0.20 g, 6.0 mmol) and H_2O (0.1 mL) were added. The reaction mixture was stirred at room temperature for 2 h and then concentrated *in vacuo* to provide **C180** (76 mg, crude) as a colorless oil. The oil was used directly in the next step without further purification.

Step 4. Preparation of ethyl 5-(5-(2-(dimethylamino)-2-oxoethyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C181)**

To a solution of **C180** (78 mg, 0.21 mmol) in DMF (5.0 mL) was added HATU (0.13 g, 0.34 mmol), DIEA (0.15 g, 1.1 mmol), and dimethylamine hydrochloride (CAS: 506-59-2; 28 mg, 0.34 mmol). The reaction mixture was stirred at room temperature for 1 h, diluted with H_2O (4 mL), and extracted with EtOAc (3 x 5 mL). The organic layer was washed with brine (5 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-80% EtOAc: PE) to provide **C181** (0.12 g, 87% yield) as a yellow oil. (LC/MS) m/z $(M+H)^+$ = 400.3.

Step 5. Preparation of 5-(5-(2-(dimethylamino)-2-oxoethyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C182)**

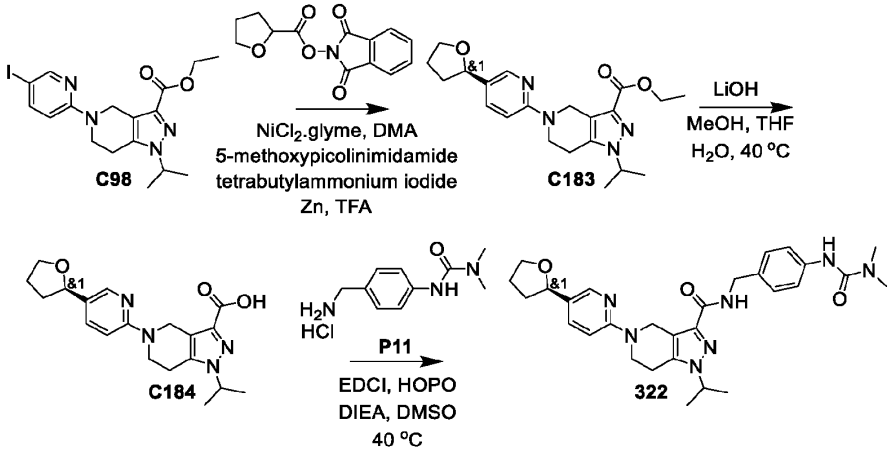
To a solution of **C181** (0.12 g, 0.30 mmol) in THF (4.0 mL), MeOH (0.5 mL), and H_2O (1.0 mL) was added LiOH (22 mg, 0.90 mmol). The reaction mixture was then stirred at 40 °C for 3 h then was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (0.05% formic acid)/ Mobile Phase B: ACN, 0 to 34% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **C182** (35 mg, 31% yield) as a white solid.

Step 6. Preparation of 5-(5-(2-(dimethylamino)-2-oxoethyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(286)**

To a solution of **C182** (35 mg, 0.094 mmol) in DMSO (3.0 mL) was added DIEA (61 mg, 0.47 mmol), EDCI (43 mg, 0.23 mmol), and HOPO (31 mg, 0.28 mmol). The reaction mixture was stirred at 40 °C for 15 min, and then **P11** (26 mg, 0.11 mmol) was added. The suspension was stirred at 40 °C for 12 h then purified by HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/Mobile Phase B: ACN, 5 to 45% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 60 mL/min) to provide **286** (26 mg, 50% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 547.3. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 – 8.16 (m, 2H), 7.91 (s, 1H), 7.35 (d, 3H), 7.14 (d, 2H), 6.79 (d, 1H), 4.60 (s, 2H), 4.50 – 4.37 (m, 1H), 4.35 – 4.27 (m, 2H), 3.89 – 3.76 (m, 2H), 3.53 – 3.44 (m, 2H), 2.97 (s, 3H), 2.87 (s, 6H), 2.80 – 2.70 (m, 5H), 1.35 (d, 6H).

Example 322

rac-(R)-N-(4-(3,3-Dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(322)**



Step 1. Preparation of *rac*-ethyl (*R*)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C183)**

A reaction mixture of $NiCl_2$.glyme (59.9 mg, 0.273 mmol) and 5-methoxypicolinimidamide (41.2 mg, 0.273 mmol) in DMA (1.4 mL) was stirred at room temperature for 2 min before **C98** (0.120 g, 0.273 mmol) and 1,3-dioxoisoindolin-2-yl tetrahydrofuran-2-carboxylate (CAS: 1872262-69-5; 0.107 g, 0.409 mmol) were added. The reaction mixture was stirred for 2 min then tetrabutylammonium iodide (CAS: 311-28-4; 0.101 g, 0.273 mmol), preactivated Zn (0.125 g, 1.91 mmol), and TFA (15.5 mg, 0.136 mmol) were added. The suspension was stirred at room temperature for 16 h and then diluted with H_2O (30 mL) and EtOAc (20 mL). The mixture was filtered through Celite. The filtrate was concentrated *in vacuo* and the residue was purified by reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/Mobile Phase B: ACN, 39 to 59% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 60 mL/min) to provide **C183** (25.1 mg, 26.6% yield) as a gum. (LC/MS) m/z $(M+H)^+$ = 385.2. ^1H NMR (400 MHz, CD_3OD) δ 8.09 (d, 1H), 7.59 (dd, 1H), 6.89 (d, 1H), 4.81 – 4.73 (m, 1H), 4.67 (s, 2H), 4.63 – 4.48 (m, 1H), 4.40 (q, 2H), 4.11 – 4.01 (m, 1H), 3.96 (t, 2H), 3.93 – 3.84 (m, 1H), 2.86 (t, 2H), 2.35 – 2.23 (m, 1H), 2.12 – 1.98 (m, 2H), 1.87 – 1.73 (m, 1H), 1.52 – 1.36 (m, 9H).

Step 2. Preparation of *rac*-(*R*)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C184)**

To a solution of **C183** (23.7 mg, 0.616 mmol) in THF (1.0 mL), MeOH (0.5 mL), and H_2O (0.5 mL) was added LiOH (7.76 mg, 0.185 mmol). The reaction mixture was stirred at 40 °C for 3 h, and then 2M HCl was added to pH~5. The acidic yellow solution was concentrated *in vacuo* then lyophilized to form **C184** (22.0 mg, crude) as a light brown solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 357.1

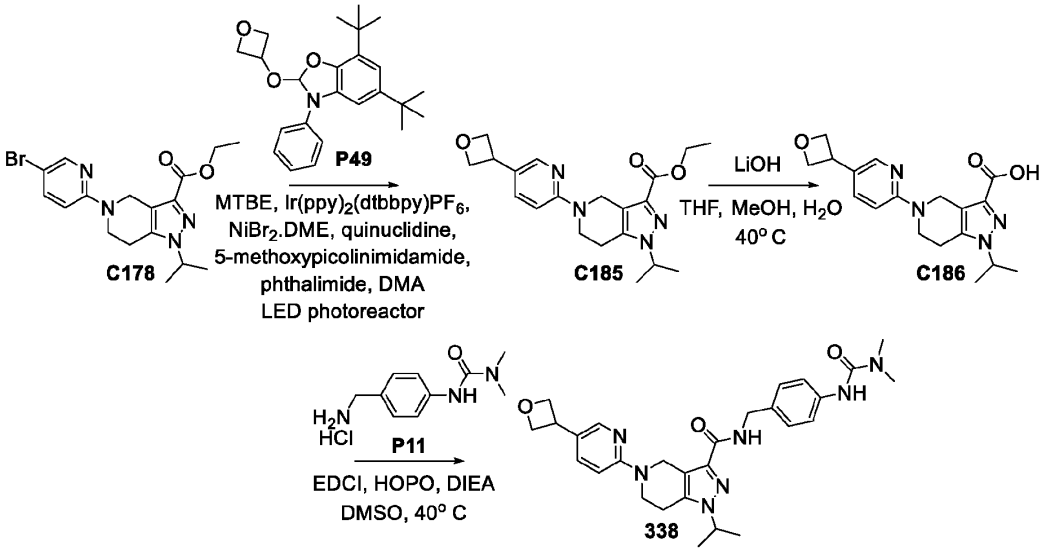
Step 3. Preparation of *rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(322)**

A reaction mixture of **C184** (22.0 mg, 0.0617 mmol), HOPO (20.6 mg, 0.185 mmol), EDCI (28.4 mg, 0.148 mmol), and DIEA (39.9 mg, 0.309 mmol) in DMSO (1.0 mL) was stirred at 40 °C for 30 min. The suspension was added **P11** (21.3 mg, 0.0926 mmol), and then the reaction mixture was stirred at 40 °C for 6 h. The yellow reaction mixture was purified with reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/Mobile Phase B: ACN, 16 to 56% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **322** (18.4 mg, 55.9% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 532.2. ^1H NMR (400 MHz, CD_3OD) δ 8.10 (d, 1H), 7.61 (dd, 1H), 7.39 – 7.35 (m, 2H), 7.34 – 7.28 (m, 2H), 6.91 (d, 1H), 4.81 – 4.76 (m, 1H), 4.70 (s, 2H), 4.56 – 4.50 (m, 3H), 4.12 – 3.87 (m, 4H), 3.05 – 3.03 (m, 6H), 2.87 (t, 2H), 2.36 – 2.24 (m, 1H), 2.15 – 2.00 (m, 2H), 1.90 – 1.77 (m, 1H), 1.49 (d, 6H). The chiral purity was determined

using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; isocratic: 40% of Mobile Phase B; flow rate: 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to show a mixture of peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 532.16 at retention time: 0.734 min, 49.42% ee) and peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 532.17 at retention time: 1.055 min, 50.58% ee).

Example 338

N-(4-(3,3-Dimethylureido)benzyl)-1-isopropyl-5-(5-(oxetan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(338)**



Step 1. Preparation of ethyl 1-isopropyl-5-(5-(oxetan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C185)**

In a glovebox, to **C178** (0.100 g, 0.254 mmol) was added $Ir(ppy)_2(dtbbpy)PF_6$ (CAS: 676525-77-2; 3.49 mg, 0.00381 mmol), $NiBr_2$.DME (7.85 mg, 0.0254 mmol), 5-methoxypicolinimidamide (CAS: 1179532-65-0; 3.84 mg, 0.0254 mmol), phthalimide (9.35 mg, 0.0636 mmol), quinuclidine (49.5 mg, 0.445 mmol), and DMA (3 mL). A solution of **P49** (194 mg, 0.509 mmol) in MTBE (3 mL) was added to the suspension via a syringe with a filter. The reaction vessel was sealed and irradiated with a photoreactor (maximum fan speed; stirred speed: 1500 rpm; 100% light intensity LED) for 16 h. The reaction mixture was concentrated *in vacuo,* then basified with aqueous NH_4OH and diluted with MeOH (1 mL). The solution was purified by reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/Mobile Phase B: ACN, 21 to 61% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 60 mL/min) to provide **C185** (25.1 mg, 26.6% yield) as a gum. (LC/MS) m/z $(M+H)^+$ = 371.3. ^1H NMR (400 MHz, CD_3OD) δ 8.05 (d, 1H), 7.78 (dd, 1H), 6.93 (d, 1H), 5.03 (dd, 2H), 4.71 – 4.62 (m, 4H), 4.60 – 4.46 (m, 1H), 4.38 (q, 2H), 4.23 – 4.11 (m, 1H), 3.94 (t, 2H), 2.84 (t, 2H), 1.45 (d, 6H), 1.41 (t, 3H).

Step 2. Preparation of 1-isopropyl-5-(5-(oxetan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C186)**

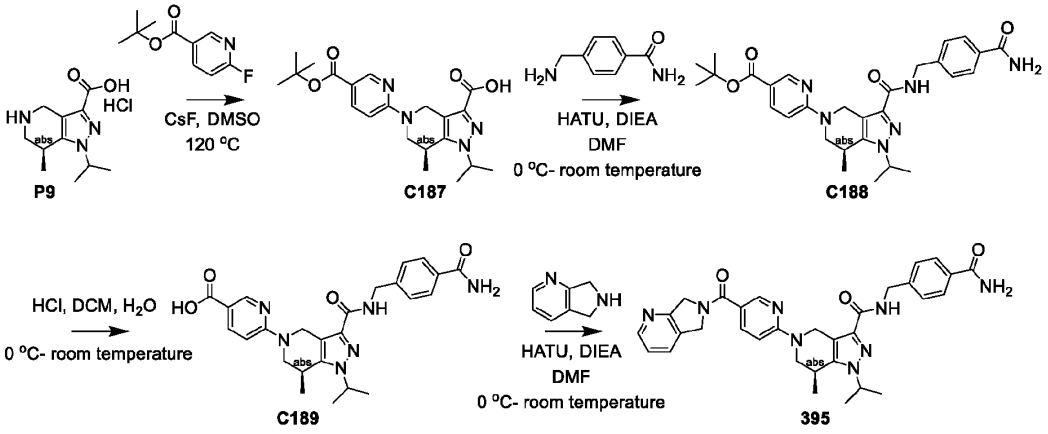
To a solution of **C185** (25.1 mg, 0.0678 mmol) in THF (1.0 mL), MeOH (0.5 mL), and H_2O (0.5 mL) was added LiOH (8.53 mg, 0.203 mmol). The reaction mixture was then stirred at 40 °C for 2.5 h and then concentrated *in vacuo*. The residue was diluted with H_2O (0.5 mL), and then the pH was adjusted with diluted formic acid in H_2O to pH=6. The resulting yellow solution was lyophilized under high vacuum to provide **C186** (23.2 mg, crude) as a light brown solid. This solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 343.2.

Step 3. Preparation of *N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(oxetan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(338)**

A reaction mixture of **C186** (23.2 mg, 0.0678 mmol), HOPO (22.6 mg, 0.203 mmol), EDCI (31.2 mg, 0.163 mmol), and DIEA (43.8 mg, 0.339 mmol) in DMSO (2.0 mL) was stirred at 40 °C for 30 min. **P11** (23.4 mg, 0.102 mmol) was added to the suspension, and then the reaction mixture was stirred at 40 °C for 8 h. The yellow reaction mixture was purified with reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (NH_4OH-NH_4HCO_3)/Mobile Phase B: ACN, 9 to 52% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 2 min, flow rate: 30 mL/min) and lyophilized to provide **338** (6.51 mg, 18.6% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 518.3. ^1H NMR (400 MHz, CD_3OD) δ 8.06 (d, 1H), 7.79 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.30 – 7.25 (m, 2H), 6.94 (d, 1H), 5.08 – 5.01 (m, 2H), 4.72 – 4.65 (m, 4H), 4.55 – 4.47 (m, 3H), 4.23 – 4.14 (m, 1H), 3.97 (t, 2H), 3.00 (s, 6H), 2.84 (t, 2H), 1.45 (d, 6H).

Example 395

(*S*)-*N*-(4-Carbamoylbenzyl)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(395)**



Step 1. Preparation of (*S*)-5-(5-(*tert*-butoxycarbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C187)**

To a reaction mixture of **P9** (0.10 g, 0.45 mmol) and CsF (0.17 g, 1.1 mmol) in DMSO (4 mL) was added *tert*-butyl 6-fluoronicotinate (CAS: 676560-01-3, 88 mg, 0.45 mmol) and then stirred at 120 °C for 16 h. The reaction mixture was diluted with H_2O (5 mL) and then extracted with (1:10, MeOH: DCM, 3 x 2 mL). The combined organic layer was washed with brine (2 x 3 mL), dried with Na_2SO_4, filtered, and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-20% EtOAc: PE) to provide **C187** (55 mg, 31% yield) as a yellow oil. (LCMS) *m/z* $(M+H)^+$ = 401.2.

Step 2. Preparation of *tert*-butyl (*S*)-6-(3-((4-carbamoylbenzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinate **(C188)**

At 0 °C, to a solution of **C187** (55 mg, 0.14 mmol) in DMF (2 mL) was added HATU (52 mg, 0.14 mmol) and then stirred for 30 min. Then DIEA (71 mg, 0.55 mmol) and **P11** (26 mg, 0.14 mmol) were added. The reaction mixture was stirred at room temperature for 2 h and then poured into ice water (4 mL). The suspension was filtered, and the filter cake was collected to provide **C188** (65 mg, 89% yield) as a solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 533.3.

Step 3. Preparation of (*S*)-6-(3-((4-carbamoylbenzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinic acid hydrochloride **(C189)**

At 0 °C, to a solution of **C188** (0.14 g, 0.26 mmol) in DCM (2 mL) was added 2N HCl in dioxane (2 mL) and then stirred for 4 h. The reaction mixture was concentrated *in vacuo* to provide **C189** (67 mg, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 477.1.

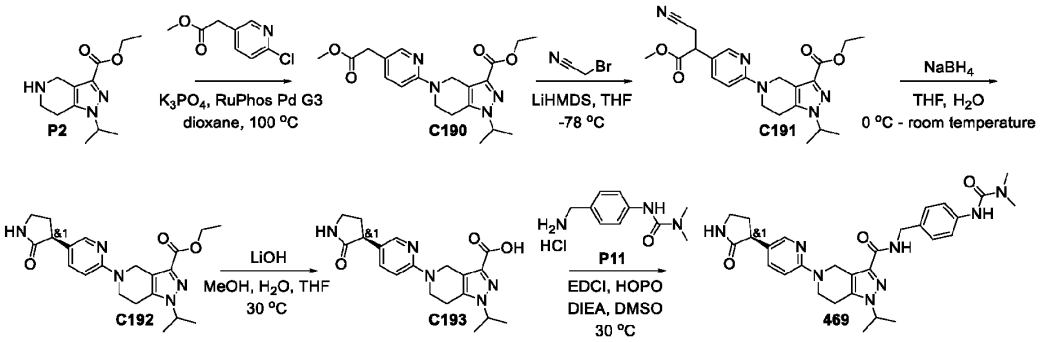
Step 4. Preparation of (*S*)-*N*-(4-carbamoylbenzyl)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(395)**

To a solution of **C189** (67 mg, 0.13 mmol) in DMF (2 mL) was added HATU (0.050 g, 0.13 mmol). The reaction mixture was stirred at 0 °C for 30 min, then DIEA (67 mg, 0.52 mmol) and 6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine (CAS: 147739-88-6; 16 mg, 0.13 mmol) were added. The suspension was stirred for 2 h at room temperature, poured into ice water (8 mL), and extracted with EtOAc (3 x 5 mL). The combined organic layer was washed with Na_2CO_3 (2 x 5 mL) and brine (10 mL), dried with Na_2SO_4, and then concentrated *in vacuo*. The residue was dissolved in DMF then purified by reverse phase HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 µm column; Mobile Phase A: H_2O (0.05% formic acid)/ Mobile Phase B: ACN, 25 to 45% of Mobile Phase B over 10 min, held at 100% of Mobile Phase B for 2 min; flow rate: 35 mL/min) and lyophilized to provide **395** (19 mg, 25% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ = 579.4.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.55 (t, 1H), 8.50 – 8.41 (m, 2H), 7.92 – 7.75 (m, 5H), 7.36 (d, 2H), 7.32 – 7.26 (m, 2H), 6.95 – 6.90 (m, 1H), 5.12 (d, 1H), 4.99 – 4.78 (m, 4H), 4.60 – 4.40 (m, 4H), 4.25 (d, 1H), 3.28 – 3.20 (m, 2H), 1.47 – 1.38 (m, 6H), 1.20 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak AS-3 50 x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: EtOH containing 0.2% NH_3; Isocratic: 40% of Mobile phase B; backpressure: 1500 psi; flow rate: 3.0 mL/min; column temperature: 35 °C to provide Example **395**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 579.19 at retention time: 1.586 minutes, 98% ee)

Example 469

rac-(*R*)-*N*-(4-(3,3-Dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(469)**



Step 1. Preparation of ethyl 1-isopropyl-5-(5-(2-methoxy-2-oxoethyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C190)**

A reaction mixture of methyl 2-(6-chloropyridin-3-yl)acetate (CAS: 717106-69-9; 1.40 g, 7.54 mmol), **P2** (2.17 g, 7.92 mmol), K_3PO_4 (4.80 g, 22.6 mmol) and RuPhos Pd G3 (0.631 g, 0.754 mmol) in dioxane (50 mL) was degassed with nitrogen gas for 2 min. The reaction mixture was stirred at 100 °C for 24 h and then filtered. The filter cake was washed with EtOAc. The filtrate was purified by column chromatography (silica gel, 0-62% EtOAc: PE) to give **C190** (2.22 g, 76.2% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, 1H), 7.45 (dd, 1H), 6.72 (d, 1H), 4.62 (s, 2H), 4.54 – 4.38 (m, 3H), 4.08 – 4.03 (m, 2H), 3.68 (s, 3H), 3.50 (s, 2H), 2.81 (t, 2H), 1.52 (d, 6H), 1.42 (t, 3H).

Step 2. Preparation of ethyl 5-(5-(3-cyano-1-methoxy-1-oxopropan-2-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C191)**

At -78 °C under nitrogen gas, to a solution of **C190** (1.72 g, 4.45 mmol) in THF (22 mL) was added LiHMDS (1.12 g, 6.68 mmol). The reaction mixture was stirred at -78 °C for 30 min under nitrogen gas, and then 2-bromoacetonitrile (CAS: 590-17-0; 0.667 g, 5.56 mmol) was added dropwise. The suspension was stirred at -78 °C for 2 h and quenched with NH_4Cl (20 mL). The reaction mixture was extracted with EtOAc (3x). The combined organic phase was

washed with brine and then dried with Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo* then purified by column chromatography (silica gel, 0-50% EtOAc: PE) to provide **C191** (1.70 g, 69.6% yield) as a yellow gum. (LCMS) *m/z* $(M+H)^+$ = 426.2. ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, 1H), 7.43 (dd, 1H), 6.74 (d, 1H), 4.65 (s, 2H), 4.55 – 4.38 (m, 3H), 4.17 – 4.05 (m, 2H), 3.89 – 3.80 (m, 1H), 3.72 (s, 3H), 2.98 (dd, 1H), 2.86 – 2.74 (m, 3H), 1.52 (d, 6H), 1.42 (t, 3H).

Step 3. Preparation of *rac*-ethyl (*R*)-1-isopropyl-5-(5-(2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C192)**

The reaction was conducted in two batches combined for the work-up and purification. At 0 °C, under nitrogen gas, to a solution of **C191** (1.50 g, 3.52 mmol) in THF (20 mL) and H_2O (3 mL), $NaBH_4$ (0.534 g, 14.1 mmol) was slowly added to form the first batch. The reaction mixture of the first batch was stirred for 3 h at room temperature and then quenched with saturated NH_4Cl (20 mL) and filtered through Celite.

A second batch of the same reaction was conducted with **C191** (0.200 g, 0.470 mmol). The two batches were combined and extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with brine (10mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-65% EtOAc: PE) to provide **C192** (0.920 g, 58.0% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ = 398.2. ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, 1H), 7.45 (dd, 1H), 6.75 (d, 1H), 4.64 (s, 2H), 4.54 – 4.38 (m, 3H), 4.07 (t, 2H), 3.92 – 3.80 (m, 2H), 3.16 – 3.05 (m, 1H), 2.87 – 2.77 (m, 3H), 2.69 (dd, 1H), 1.70 – 1.66 (m, 1H), 1.52 (d, 6H), 1.43 (t, 3H).

Step 4. Preparation of *rac*-(*R*)-1-isopropyl-5-(5-(2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C193)**

The same reaction was conducted in two batches and combined for the work-up. To a solution of **C192** (0.13 g, 0.33 mmol) in THF (20.0 mL), H_2O (3.0 mL), and MeOH (0.5 mL) was added LiOH (69 mg, 1.6 mmol) to form the first batch. The reaction mixture of the first batch was stirred at 30 °C for 3 h, and then the second batch of the same reaction was conducted with **C192** (0.020 g, 0.050 mmol). The two batches were combined then the pH was adjusted to pH~3 with 2M aqueous HCl. The aqueous phase was concentrated *in vacuo* to provide **C193** (0.14 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LCMS) *m/z* $(M+H)^+$ = 370.1. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 12.64 (br s, 1H), 7.98 (d, 1H), 7.46 (dd, 1H), 6.81 (d, 1H), 5.00 (t, 1H), 4.56 (s, 2H), 4.50 – 4.37 (m, 1H), 3.80 (t, 2H), 3.49 – 3.38 (m, 2H), 2.92 – 2.78 (m, 2H), 2.77 – 2.66 (m, 3H), 1.30 (d, 6H).

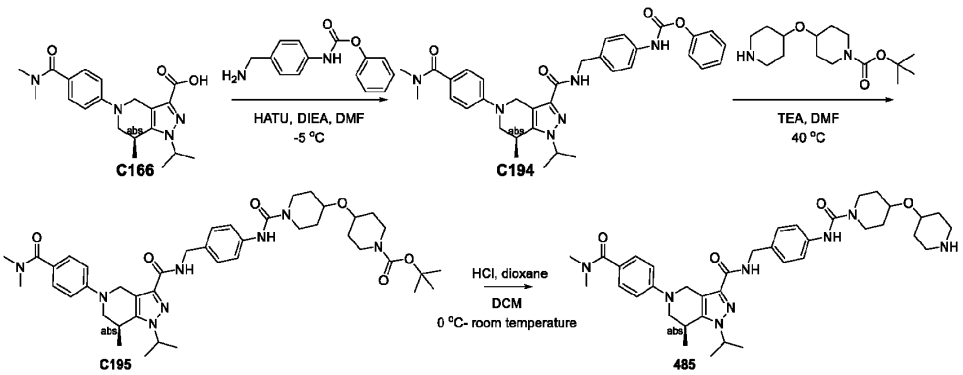
Step 5. Preparation of *rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(469)**

The same reaction was conducted in two batches and then combined for purification. To a reaction mixture of **C193** (0.11 g, 0.30 mmol) in DMSO (3 mL) was added DIEA (0.38 g, 3.0 mmol), HOPO (99 mg, 0.89 mmol), and EDCI (0.14 g, 0.71 mmol) for the first batch. The suspension was stirred at 30 °C for 15 min, and then **P11** (0.10 g, 0.45 mmol) was added to form the first batch. The reaction mixture of the first batch was stirred at 30 °C for 5 h.

The second batch of the same reaction was conducted with **C193** (0.020 g, 0.054 mmol). The two batches were combined then purified reverse phase HPLC (C_{18} 150 mm x 40 mm x 5 µm column, Mobile Phase A: H_2O (0.05% formic acid)/Mobile Phase B: ACN, 5 to 35% of Mobile Phase B over 9 min then held at 100% of Mobile Phase B for 2 min; flow rate= 60 mL/min) and lyophilized to provide **469** (0.080 g, 41.7% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 545.3. ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, 1H), 7.40 (dd, 1H), 7.37 – 7.33 (m, 2H), 7.31 – 7.27 (m, 2H), 7.16 (t, 1H), 6.79 (d, 1H), 6.32 (s, 1H), 4.70 (s, 2H), 4.55 (d, 2H), 4.42 – 4.31 (m, 1H), 4.08 (t, 2H), 3.93 – 3.76 (m, 2H), 3.12 – 3.00 (m, 7H), 2.86 – 2.75 (m, 3H), 2.71 – 2.60 (m, 1H), 1.44 (d, 6H). The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: EtOH containing 0.2% NH_3; Isocratic: 40% of Mobile phase B; backpressure: 1500 psi; flow rate: 4.0 mL/min; column temperature: 35 °C to show a mixture of peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 545.55 at retention time: 1.006 minutes, 49.54% ee) and peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 545.55 at retention time: 1.470 min, 50.46% ee).

Example 485

(*S*)-5-(4-(Dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-(piperidin-4-yloxy)piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide hydrochloride **(485)**



Step 1. Preparation of phenyl (*S*)-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate **(C194)**

At -5 °C, to a reaction mixture of **C166** (1.20 g, 3.24 mmol) and phenyl (4-(aminomethyl)phenyl)carbamate (CAS: 1019455-66-3; 0.957 g, 3.43 mmol) in DMF (16 mL) was added HATU (1.29 g, 3.40 mmol). The reaction mixture was stirred at -5 °C for 10 min, and then DIEA (1.67 g, 13.0 mmol) was added. The suspension was stirred at -5 °C for 1 h then was poured into ice water and filtered. The filter cake was washed with H_2O (3 x 15 mL) and lyophilized to provide **C194** (1.73 g, 90.0% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 595.8. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 10.20 – 10.15 (m, 1H), 8.45 – 8.37 (m, 1H), 7.47 – 7.37 (m, 4H), 7.36 – 7.17 (m, 7H), 6.96 (d, 2H), 4.58 – 4.50 (m, 2H), 4.37 (d, 2H), 4.10 (d, 1H), 3.85 – 3.77 (m, 1H), 3.22 – 3.17 (m, 2H), 2.95 (s, 6H), 1.42 (dd, 6H), 1.28 (d, 3H).

Step 2. Preparation of *tert*-butyl (*S*)-4-((1-((4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamoyl)piperidin-4-yl)oxy)piperidine-1-carboxylate **(C195)**

To a solution of **C194** (0.300 g, 0.504 mmol) in DMF (3 mL) were added TEA (0.204 g, 2.02 mmol) and *tert*-butyl 4-(piperidin-4-yloxy)piperidine-1-carboxylate (CAS: 845305-83-1; 0.143 g, 0.504 mmol). The reaction mixture was stirred at 40 °C for 2 h then poured into H_2O and filtered. The filter cake was washed with H_2O (3 x 15 mL) and lyophilized to provide **C195** (0.360 g, 90.9% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 785.5.

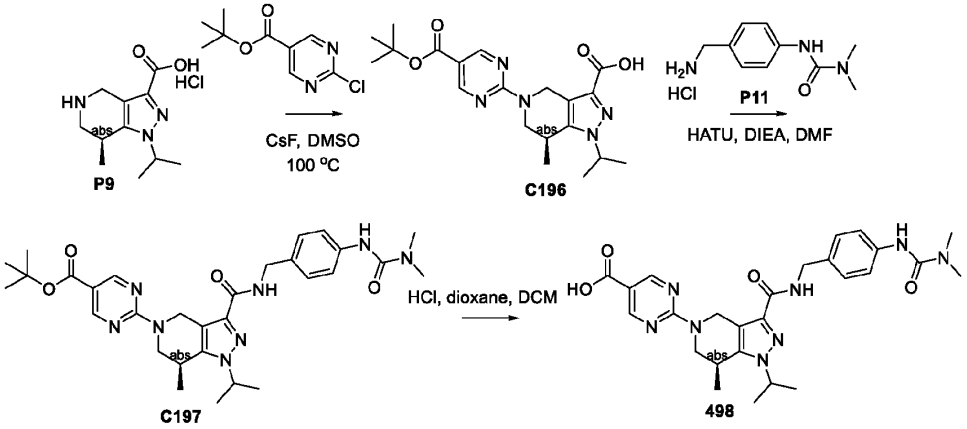
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Step 3. Preparation of (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-(piperidin-4-yloxy)piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide hydrochloride (**485**)

At 0 °C, to a solution of **C195** (0.361 g, 0.460 mmol) in DCM (5 mL) was added 2M HCl in dioxane (15 mL). The reaction mixture was stirred at room temperature for 2 h then concentrated *in vacuo*. The residue was diluted with H_2O then purified by reverse phase HPLC (Boston Green ODS 150 mm x 30 mm x 5 μm column; Mobile phase: A: H_2O (0.05% aqueous HCl)/ Mobile Phase B: ACN; 15-55% of Mobile Phase B over 9.0 min; flow rate: 30 mL/ min) and lyophilized to provide **485** (18.7 mg, 37.3% yield) as a yellow solid. (LC/MS) m/z $(M+H)^+$ = 685.5. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.70 – 8.50 (m, 2H), 8.42 – 8.34 (m, 1H), 8.24 (t, 1H), 7.31 – 7.19 (m, 4H), 7.12 – 7.05 (m, 2H), 6.89 – 6.83 (m, 2H), 4.50 – 4.38 (m, 2H), 4.31 – 4.19 (m, 2H), 4.00 (d, 1H), 3.76 – 3.59 (m, 4H), 3.58 – 3.50 (m, 1H), 3.21 – 2.93 (m, 6H), 2.92 – 2.80 (m, 8H), 1.86 – 1.77 (m, 2H), 1.74 – 1.66 (m, 2H), 1.60 – 1.48 (m, 2H), 1.37 – 1.25 (m, 7H), 1.18 (d, 3H).

Example 498

(*S*)-2-(3-((4-(3,3-Dimethylureido)benzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyrimidine-5-carboxylic acid **(498)**



Step 1. Preparation of (*S*)-5-(5-(*tert*-butoxycarbonyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C196)**

To a solution of **P9** (0.400 g, 1.54 mmol) and CsF (585 mg, 3.85 mmol) in DMSO (15 mL) was added *tert*-butyl 2-chloropyrimidine-5-carboxylate (CAS: 1864223-07-3; 331 mg, 1.54 mmol). The reaction mixture was stirred at 100 °C for 2 h and then diluted with H_2O (15 mL). The suspension was extracted with EtOAc (3 x 15 mL). The combined organic layer was washed with brine (3 x 40 mL) and then dried with Na_2SO_4 and concentrated *in vacuo* to provide **C196** (0.610 g, crude) as a white solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 402.2.

Step 2. Preparation of *tert*-butyl (*S*)-2-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyrimidine-5-carboxylate **(C197)**

To a solution of **C196** (0.610 g, 1.52 mmol) and **P11** (349 mg, 1.52 mmol) in DMF (15 mL) was added HATU (607 mg, 1.60 mmol) and DIEA (786 mg, 6.08 mmol). The reaction mixture was stirred at room temperature for 30 min then was diluted with H_2O (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (3 x 60 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by column chromatography (silica gel, 0-70% EtOAc: hexane) then lyophilized to provide **C197** (0.780 g, 89.0% yield) as a solid. ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.76 (s, 2H), 8.36 (t, 1H), 8.22 (s, 1H), 7.44 – 7.32 (m, 2H), 7.23 – 7.12 (m, 2H), 5.54 (d, 1H), 4.58 – 4.46 (m, 1H), 4.42 – 4.25 (m, 3H), 3.47 – 3.38 (m, 3H), 2.95 – 2.88 (m, 6H), 1.51 (s, 9H), 1.40 (dd, 6H), 1.10 (d, 3H).

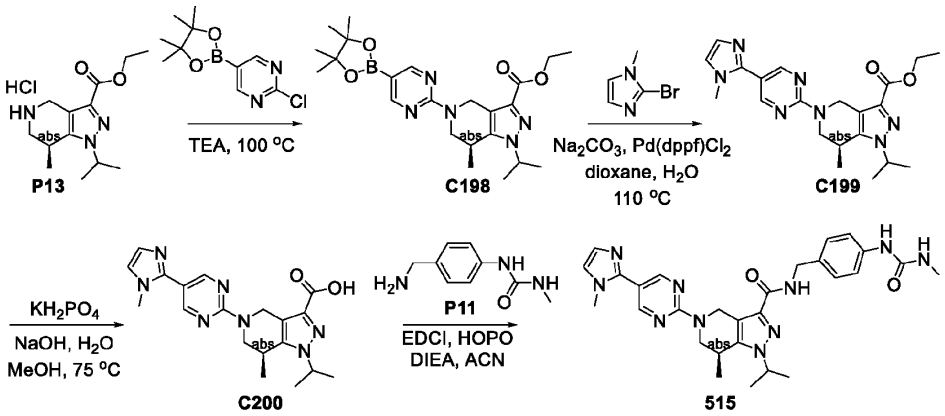
Step 3. Preparation of (*S*)-2-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyrimidine-5-carboxylic acid **(498)**

To a solution of **C197** (0.780 g, 1.35 mmol) in DCM (3 mL) was added 2 M HCl in dioxane (20 mL). The reaction mixture was then stirred at room temperature for 5 h then concentrated *in vacuo* and lyophilized to provide **498** (0.701 g, crude) as a solid. The solid was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 521.3. ^1H NMR

(400 MHz, $(CD_3)_2SO$) δ 8.80 (s, 2H), 8.36 (t, 1H), 8.24 (s, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 5.54 (d, 1H), 4.81 (d, 1H), 4.57 – 4.46 (m, 1H), 4.40 – 4.27 (m, 3H), 3.49 – 3.41 (m, 1H), 3.32 – 3.22 (m, 1H), 2.94 – 2.86 (m, 6H), 1.41 (dd, 6H), 1.13 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralcel OJ-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; gradient: 5-40% of Mobile Phase B over 1.5 min then held at 40% of Mobile Phase B for 1.0 min then 5% of Mobile Phase B for 0.5 min; flow rate: 3.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **498**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 521.48 at retention time: 1.543 min, 100% ee).

Example 515

(*S*)-1-Isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(515)**



Step 1. Preparation of ethyl (*S*)-1-isopropyl-7-methyl-5-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C198)**

To a reaction mixture of **P13** (0.598 g, 2.08 mmol) and TEA (0.463 g, 4.57 mmol) in dioxane (5.0 mL) was added 2-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidine (CAS: 1003845-08-6; 0.500 g, 2.08 mmol). The suspension was stirred at 100 °C for 2 h and then filtered. The filter cake was rinsed with dioxane (2.5 mL). The filtrate was diluted with saturated $NaHCO_3$ and extracted with EtOAc (2 x 25 mL). The combined organic layer was washed with brine (25 mL) then dried with Na_2SO_4 and concentrated *in vacuo* to give **C198** (0.865 g, crude), which was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 456.4.

Step 2. Preparation of ethyl (*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C199)**

In a 2-neck round bottom flask was attaced a reflux condenser, to a reaction mixture of **C198** (0.865 g, 1.90 mmol) in dioxane (17.6 mL) and H_2O (2.3 mL) was added Na_2CO_3 (0.604 g, 5.70 mmol) and 2-bromo-*N*-methylimidazole (CAS: 16681-59-7; 0.352 g, 2.18 mmol), reaction was purged with nitrogen gas for a few minutes. The reaction mixture was added Pd(dppf)Cl_2 (0.155 g, 0.190 mmol) and degassed with nitrogen gas. The suspension was stirred at 110 °C for ~24 h and filtered over celite. The filter cake was washed with EtOAc (40 mL). The filtrate was concentrated *in vacuo* then purified by column chromatography (silica gel, 0-10% MeOH: DCM) then dried further over high vacuum to provide **C199** (0.779 g, >95.0% yield). (LC/MS) m/z $(M+H)^+$ = 410.3.

Step 3. Preparation of (*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C200)**

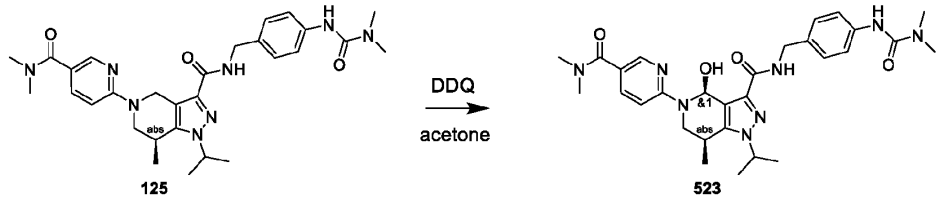
To a stirred solution of **C199** (0.779 g, 1.90 mmol) in MeOH (2.1 mL) was added 1M NaOH in H_2O (4.2 mL). The reaction mixture was stirred at 75 °C for 20 h before KH_2PO_4 (0.828 g, 6.09 mmol) was added and then cooled to room temperature. The suspension was concentrated *in vacuo* to remove the MeOH. Brine (10 mL) was added to the aqueous layer extracted with DCM (2 x 20 mL). The combined organic layer was dried with Na_2SO_4 and then concentrated *in vacuo* to provide **C200** (0.419 g, 57.7% yield) as a brown oil. (LC/MS) m/z $(M+H)^+$ = 382.3.

Step 4. Preparation of (*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(515)**

To a reaction mixture of **P11** (51.7 mg, 0.288 mmol), HOPO (35.0 mg, 0.315 mmol), EDCI (75.4 mg, 0.393 mmol), **C200** (0.100 g, 0.262 mmol) in ACN (1.3 mL) was added DIEA (0.102 g, 0.786 mmol) then stirred at room temperature for ~24 h. The suspension was filtered. The filter cake and filtrate were combined then concentrated *in vacuo*. The residue was purified reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/Mobile Phase B: ACN (0.05% TFA), 70 to 80% of Mobile Phase B over 10 min, flow rate= 25 mL/min) and lyophilized to provide **515** (36.4 mg, 25.6% yield). (LC/MS) m/z $(M+H)^+$ = 543.5. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.77 (s, 1H), 8.44 (s, 1H), 8.38 (t, 1H), 7.81 – 7.77 (m, 2H), 7.34 – 7.30 (m, 2H), 7.19 – 7.15 (m, 2H), 5.97 – 5.93 (m, 1H), 5.55 (d, 1H), 4.82 (d, 1H), 4.57 – 4.50 (m, 1H), 4.41 – 4.28 (m, 3H), 3.87 – 3.85 (m, 3H), 3.50 – 3.47 (m, 2H), 3.34 – 3.28 (m, 1H), 2.62 (d, 3H), 1.43 (dd, 6H), 1.16 (d, 3H).

Example 523

(4*RS*,7*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4-hydroxy-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(523)**

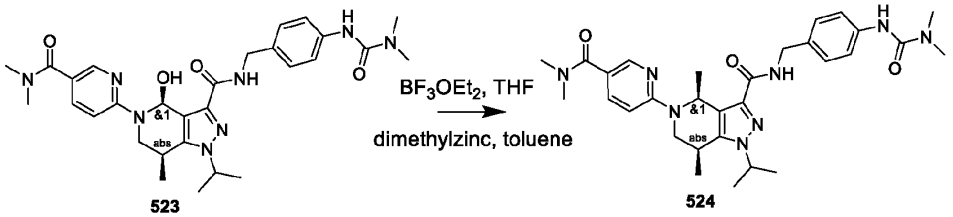


Step 1. Preparation of (4*RS*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4-hydroxy-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(523)**

To a reaction mixture of **125** (0.21 g, 0.38 mmol) in acetone (1.9 mL) was added DDQ (90 mg, 0.40 mmol). The suspension was stirred at room temperature under air for a few minutes and then diluted with saturated $NaHCO_3$ (40 mL). The mixture was extracted with DCM (40 mL), and then the organic layer was concentrated *in vacuo*. The residue was purified with SFC (Chiral Technologies OJ-H 250 mm x 30 mm x 5 µm column, Mobile Phase A: 80% CO_2/ Mobile Phase B: 20% MeOH; flow rate: 80 mL/ min; backpressure: 100 bar; column temperature: 40 °C) to provide **523** (0.090 g, 42% yield). ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.61 (t, 1H), 8.28 – 8.22 (m, 2H), 7.71 – 7.63 (m, 1H), 7.44 – 7.38 (m, 2H), 7.23 – 7.16 (m, 2H), 7.10 – 7.01 (m, 1H), 6.62 (s, 1H), 5.98 – 5.95 (m, 1H), 4.69 – 4.64 (m, 1H), 4.58 – 4.51 (m, 1H), 4.46 – 4.34 (m, 2H), 3.49 – 3.43 (m, 1H), 3.22 – 3.19 (m, 1H), 3.03 – 2.95 (m, 6H), 2.92 (s, 6H), 1.50 – 1.34 (m, 6H), 1.14 – 1.05 (m, 3H).

Example 524

(4*RS*,7*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(524)**



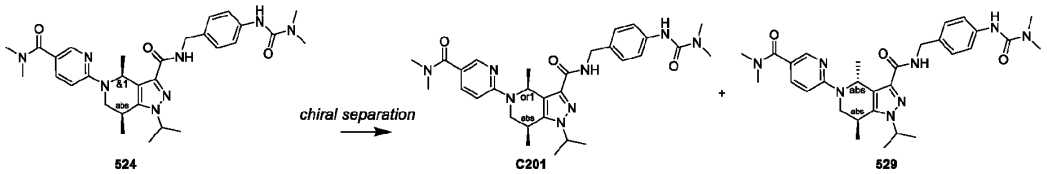
Step 1. Preparation of (4*RS*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(524)**

To a reaction mixture of **523** (0.100 g, 0.178 mmol) in THF (0.89 mL) was added BF_3OEt_2 (50.4 mg, 0.355 mmol). The suspension was stirred at room temperature for 15 min before 2M dimethylzinc in toluene (0.18 mL) was added. The reaction mixture was stirred at room temperature for ~72 h then quenched with H_2O. The suspension was extracted with DCM (3x). The combined organic layer was concentrated *in vacuo* then purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/ Mobile Phase B: ACN (0.05% TFA), 65 to 85% of Mobile Phase B over 10 min, flow rate= 25 mL/min)

and lyophilized to provide **524** (0.100 g, 100% yield). LC/MS *m/z* $(M+H)^+$ = 561.4. ^1H NMR (600 MHz, $(CD_3)_2SO$) δ 8.34 (t, 1H), 8.24 – 8.19 (m, 2H), 7.64 (d, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 6.93 (d, 1H), 5.73 (s, 1H), 4.52 – 4.46 (m, 2H), 4.43 – 4.37 (m, 1H), 4.34 – 4.27 (m, 1H), 3.42 (d, 1H), 3.23 – 3.16 (m, 1H), 2.98 (s, 6H), 2.90 (s, 6H), 1.43 – 1.36 (m, 9H), 1.13 (d, 3H).

Example 529

rel-(4*S**,7*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(C201)** and (4*R*,7*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(529)**

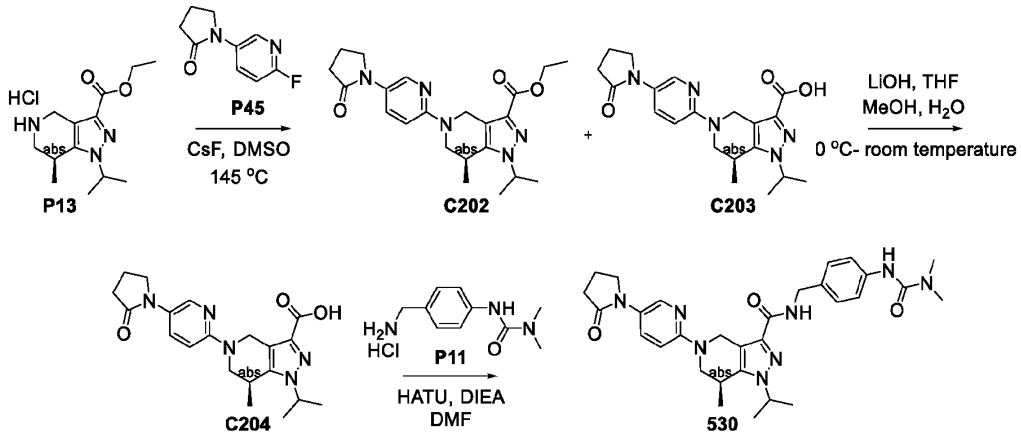


Step 1. Preparation of *rel*-(4*S**,7*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(C201)** and (4*R*,7*S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(529)**

Example **524** (0.100 g, 0.178 mmol) was purified with SFC [Column: Phenomenex Lux Cellulose 1, 250 mm x 21 mm x 5 µm; Mobile phase: 30% MeOH (0.2% NH_4OH)/ 70% ACN; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar] to provide the minor first eluting isomer as Example **C201** (0.30 mg, 3.0% yield) and the second eluting isomer as Example **529** (38 mg, 38% yield). LC/MS *m/z* $(M+H)^+$ = 561.2. ^1H NMR (600 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.21 – 8.17 (m, 2H), 7.57 (dd, 1H), 7.37 – 7.31 (m, 2H), 7.18 – 7.10 (m, 2H), 6.83 (d, 1H), 5.70 (s, 1H), 4.50 – 4.40 (m, 2H), 4.39 – 4.30 (m, 1H), 4.29 – 4.20 (m, 1H), 3.31 – 3.27 (m, 1H), 3.18 – 3.08 (m, 1H), 2.94 (s, 6H), 2.86 (s, 6H), 1.39 – 1.27 (m, 9H), 1.08 (d, 3H). The chiral purity was determined using SFC analytical method on Lux Cellulose 1, 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 60% of Mobile Phase B over 5 min; flow rate: 5.0 mL/min; backpressure: 120 bar to provide **C201**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 561.2 at retention time: 3.02 min) and Example **529:** peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 561.2 at retention time: 3.28 min, 99% ee).

Example 530

(*S*)-*N*-(4-(3,3-Dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(530)**



Step 1. Preparation of ethyl (*S*)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C202)** and (*S*)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C203)**

To a solution of **P45** (0.169 g, 0.938 mmol) and **P13** (0.270 g, 0.938 mmol) in DMSO (3 mL) was added CsF (0.855 g, 5.63 mmol). The reaction mixture was stirred at 145 °C for 48 h then diluted with H_2O (10 mL) and acidified with aqueous 1M HCl to pH=4. The suspension was extracted with EtOAc (4 x 30 mL). The combined organic layer was washed with brine (20 mL) then dried with Na_2SO_4 and concentrated *in vacuo* to provide (61: 22 according to LCMS) **C203** (LC/MS) m/z $(M+H)^+$ = 384.2 **: C202** (LC/MS) m/z $(M+H)^+$ = 412.3 (0.290 g, crude) as a yellow gum. The gum was used directly in the next step without further purification.

Step 2. Preparation of (*S*)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid **(C204)**

At 0 °C, to the solution of a mixture of **C202** and **C203** (0.29 g, 0.17 mmol) in MeOH (2 mL) and THF (2 mL) were added LiOH (15 mg, 0.35 mmol) in H_2O (1 mL). The reaction mixture was stirred at room temperature for 16 h then concentrated *in vacuo* and diluted with H_2O (10 mL). The suspension was extracted with EtOAc (2 x 10 mL). The aqueous layer was acidified with 1M aqueous HCl to pH=3. The acidic aqueous phase was extracted with (1:10) (MeOH: DCM) (2 x 20 mL). The combined organic layer was washed with brine (2 x 20 mL) then dried with Na_2SO_4 and concentrated *in vacuo* to provide **C204** (0.11 g, crude) as a yellow gum. The gum was used directly in the next step without further purification. (LC/MS) m/z $(M+H)^+$ = 384.2

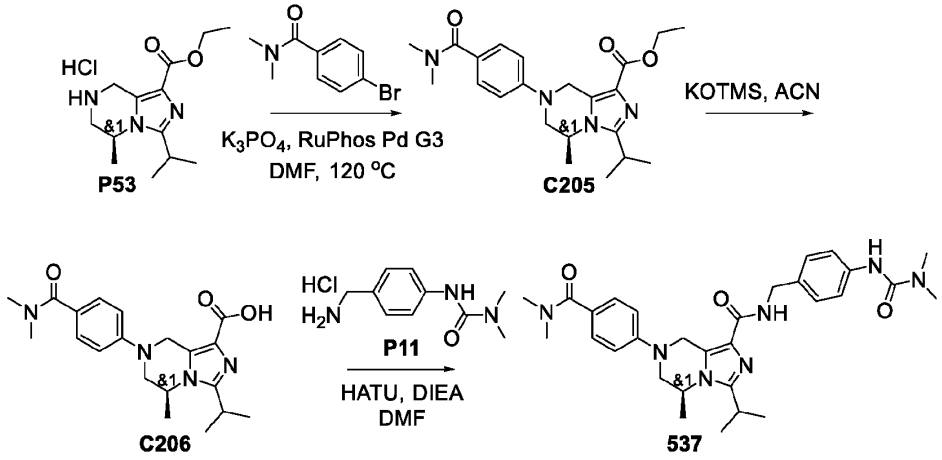
Step 3. Preparation of (*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(530)**

To a solution of **C204** (0.055 g, 0.14 mmol) and **P11** (0.033 g, 0.14 mmol) in DMF (1 mL) was added DIEA (0.074 g, 0.57 mmol) and HATU (0.057 g, 0.15 mmol). The reaction was

stirred at room temperature for 16 h then was filtered. The filtrate was purified by reverse phase HPLC (Boston Prime C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/ Mobile Phase B: ACN, 23 to 53% of Mobile Phase B over 12 min, 100% of Mobile Phase B hold 3 min, flow rate= 35 mL/min) and lyophilized to provide **530** (19 mg, 24% yield) as a white solid. (LCMS) *m/z* $(M+H)^+$ = 559.2. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.29 (d, 1H), 8.23 (s, 1H), 7.88 (dd, 1H), 7.43 – 7.35 (m, 2H), 7.21 – 7.15 (m, 2H), 6.90 (d, 1H), 4.95 (d, 1H), 4.59 – 4.48 (m, 1H), 4.40 – 4.28 (m, 3H), 4.17 (d, 1H), 3.78 (t, 2H), 3.32 – 3.18 (m, 2H), 2.91 (s, 6H), 2.44 (t, 2H), 2.12 – 2.00 (m, 2H), 1.47 – 1.38 (m, 6H), 1.21 (d, 3H). The chiral purity was determined using SFC analytical method on Chiralpak AS-3 50 x 4.6 mm x 3 µm column; Mobile phase A: CO_2/ Mobile phase B: EtOH containing 0.2% NH_3; Isocratic: 40% of Mobile phase B; backpressure: 1500 psi; flow rate: 3.0 mL/min; column temperature: 35 °C to provide Example **530**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 559.57 at retention time: 1.165 minutes, 99.53% ee)

Example 537

rac-(*R*)-7-(4-(Dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(537)**



Step 1. Preparation of *rac*-ethyl (*R*)-7-(4-(dimethylcarbamoyl)phenyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylate **(C205)**

To a reaction mixture of **P53** (0.400 g, 1.39 mmol) in DMF (10 mL) was added 4-bromo-*N,N*-dimethylbenzamide (CAS: 18469-37-9; 0.396 g, 1.74 mmol), K_3PO_4 (0.885 g, 4.17 mmol) and RuPhos Pd G3 (0.119 g, 0.142 mmol). The suspension was stirred at 120 °C under nitrogen gas for 20 h. The reaction mixture was dissolved in MeOH and filtered. The filtrate was poured into H_2O (30 mL) and extracted with EtOAc (5 x 30 mL). The combined organic layers were washed with brine (3 x 100 mL), dried with Na_2SO_4, filtered and the filtrate was concentrated *in vacuo* to give a brown gum. The gum was purified by column chromatography (silica gel, 0-4% MeOH: DCM) to provide **C205** (0.360 g, 65.0% yield) as yellow gum. (LC/MS)

m/z $(M+H)^+$ = 399.2. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.80 – 7.74 (m, 1H), 7.55 – 7.44 (m, 1H), 7.42 – 7.33 (m, 2H), 7.04 – 6.97 (m, 2H), 4.89 (d, 1H), 4.64 – 4.59 (m, 1H), 4.34 (d, 1H), 4.24 (q, 2H), 3.15 – 3.04 (m, 1H), 2.97 (s, 6H), 1.42 (d, 3H), 1.34 – 1.26 (m, 6H), 1.25 – 1.20 (m, 3H).

Step 2. Preparation of *rac*-(*R*)-7-(4-(dimethylcarbamoyl)phenyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxylic acid **(C206)**

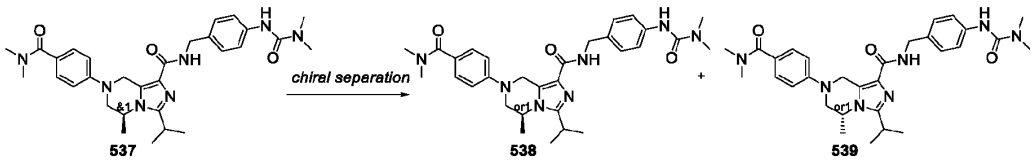
Under nitrogen gas, to a reaction mixture of **C205** (0.330 g, 0.828 mmol) in ACN (4 mL) was added KOTMS (0.319 g, 2.48 mmol). The suspension was stirred at room temperature for 2 h then acidified with 2M HCl in dioxane (0.7 mL) and concentrated *in vacuo*. The residue was diluted with brine (10 mL) and extracted with DCM (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated *in vacuo* to provide **C206** (0.280 g, 91.3% yield) as a yellow gum. (LC/MS) m/z $(M+H)^+$ = 371.2.

Step 3. Preparation of *rac*-(*R*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(537)**

To a solution of **C206** (0.280 g, 0.756 mmol) and **P11** (0.139 g, 0.605 mmol) in DMF (4 mL) was added DIEA (0.391 g, 3.02 mmol) and HATU (0.244 g, 0.642 mmol). The reaction was stirred at room temperature for 1 h then diluted with DMF and ACN. The solution was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (0.05% formic acid)/Mobile Phase B: ACN (0.05% formic acid), 24 to 44% of Mobile Phase B over 10 min, 100% of Mobile Phase B hold 2.5 min, flow rate= 30 mL/min) and lyophilized to provide **537** (0.160 g, 38.8% yield). (LCMS) *m/z* $(M+H)^+$ = 546.3. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.22 (s, 1H), 8.04 (t, 1H), 7.42 – 7.35 (m, 4H), 7.21 – 7.14 (m, 2H), 7.03 – 6.96 (m, 2H), 4.93 (d, 1H), 4.64 – 4.58 (m, 1H), 4.43 – 4.31 (m, 3H), 4.02 (d, 1H), 3.41 – 3.38 (m, 1H), 3.15 – 3.04 (m, 1H), 2.97 (s, 6H), 2.91 (s, 6H), 1.42 (d, 3H), 1.33 – 1.21 (m, 6H). The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 x 4.6 mm x 3 µm column; Mobile phase A: CO_2 / Mobile phase B: EtOH containing 0.2% NH_3; Isocratic: 40% of Mobile phase B; backpressure: 1500 psi; flow rate: 4 mL/min; column temperature: 35 °C to show a mixture of peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 546.25 at retention time: 0.609 minutes, 50.54% ee) and peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 546.22 at retention time: 1.040 minutes, 49.46% ee).

Example 538 and 539

rel-(*R* or *S*)-7-(4-(Dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(538 and 539)**

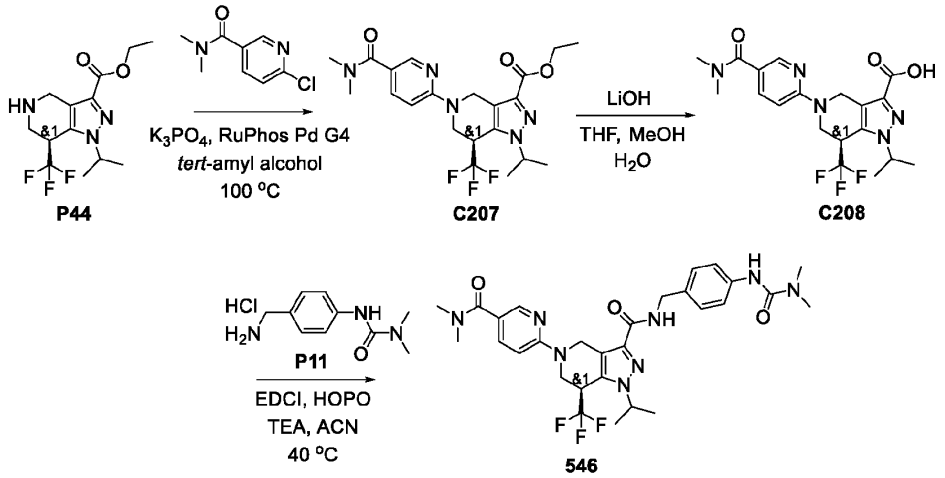


Step 1. Separation of *rel*-(*R or S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide and *rel*-(R or *S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide **(538 and 539)**

Example 537 (0.130 g, 0.238 mmol) was purified with chiral SFC [Column: Daicel chiralcel OD C_{18} 250 mm x 30 mm x 10 µm, Mobile phase: CO_2/EtOH (0.1% NH_4OH), 60% isocratic over 45 min, flow rate= 80 mL/ min] and lyophilized to provide the first eluting isomer as **539** (28.6 mg, 22.0% yield) and the second eluting isomer as **538** (27.3 mg, 21.0% yield). The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **539**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 546.24 at retention time: 0.607 min, 100% ee). ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.19 (s, 1H), 8.02 (t, 1H), 7.38 – 7.28 (m, 4H), 7.18 – 7.07 (m, 2H), 7.00 – 6.91 (m, 2H), 4.88 (d, 1H), 4.60 – 4.52 (m, 1H), 4.38 – 4.26 (m, 3H), 3.97 (d, 1H), 3.42 – 3.38 (m, 1H), 3.11 – 3.00 (m, 1H), 2.92 (s, 6H), 2.86 (s, 6H), 1.36 (d, 3H), 1.27 – 1.17 (m, 6H) and Example **538**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 546.22 at retention time: 1.034 min, 100% ee). ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.19 (s, 1H), 8.02 (t, 1H), 7.38 – 7.31 (m, 4H), 7.17 – 7.10 (m, 2H), 6.99 – 6.92 (m, 2H), 4.89 (d, 1H), 4.62 – 4.52 (m, 1H), 4.40 – 4.24 (m, 3H), 3.98 (d, 1H), 3.39 – 3.35 (m, 1H), 3.13 – 3.00 (m, 1H), 2.93 (s, 6H), 2.87 (s, 6H), 1.37 (d, 3H), 1.29 – 1.17 (m, 6H).

Example 546

rac-(*R*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(546)**



Step 1. Preparation of *rac*-ethyl (*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **(C207)**

A reaction mixture of **P44** (197 mg, 0.576 mmol), 6-chloro-*N,N*-dimethylnicotinamide (367 mg, 1.99 mmol) and K_3PO_4 (367 mg, 1.73 mmol) in *tert*-amyl alcohol (3.8 mL) was degassed with nitrogen gas for 5 min. To the suspension was added RuPhos Pd G4 (49.0 mg, 57.6 µmol). The reaction mixture was degassed with nitrogen gas for 5 min then stirred at 100 °C for 16 h. The suspension was diluted with EtOAc (10 mL) then filtered through Celite (1.5 g) prepacked on a plastic filter funnel. The filter cake was eluted with EtOAc. The filtrate was concentrated *in vacuo.* The residue was dissolved in EtOAc and heptane then concentrated *in vacuo* (2x). The solid was dissolved in DCM then purified by column chromatography (silica gel, 0-100% EtOAc: heptane) to provide **C207** (145 mg, 55.4% yield) as a light-yellow solid. (LC/MS) m/z $(M+H)^+$ = 454.6.

Step 2. Preparation of *rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylic acid

To a solution of **C207** (0.140 g, 0.308 mmol) in THF (1.47 mL), MeOH (0.15 mL) and H_2O (1.47 mL) was added LiOH (39.6 mg, 1.65 mmol) at room temperature for 2 h. The reaction mixture was quenched with 1N HCl (1.4 mL) to pH=5-6 then stirred at room temperature for 1.5 h. The reaction mixture was acidified to pH=2-3 with 1N HCl (1.7 mL) then extracted with DCM (20 mL x 1, 2 x 8 mL). The organic layers were combined then dried with Na_2SO_4, filtered, concentrated *in vacuo* and dried further under high vacuum to provide **C208** (0.144 g, crude) as a light-yellow solid. (LC/MS) m/z $(M+H)^+$ = 426.8. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, 1H), 7.73 (dd, 1H), 6.78 (d, 1H), 4.66 – 4.55 (m, 1H), 4.40 (d, 1H), 3.79 – 3.66 (m, 3H), 3.31 – 3.23 (m, 1H), 3.11 (s, 6H), 1.60 (d, 3H), 1.52 (d, 3H).

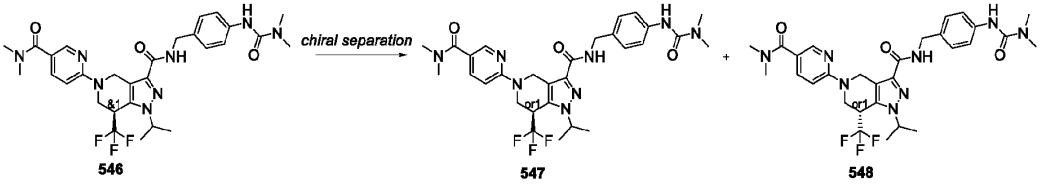
Step 3. Preparation of *rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(546)**

A reaction mixture of **C208** (0.060 g, 0.14 mmol), HOPO (19 mg, 0.17 mmol) and EDCI (41 mg, 0.21 mmol) in ACN (0.94 mL) was stirred at 40 °C for 30 min. After the stir, **P11** (36 mg, 0.16 mmol) and TEA (43 mg, 0.42 mmol) were added. The reaction mixture was stirred at room temperature for 20 h. The residue was diluted with saturated $NaHCO_3$ (8 mL) and extracted with EtOAc (3 x 8 mL). The organic layers were combined then washed with brine then dried with Na_2SO_4, filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 0-55% MeOH: EtOAc) to give **546** (73 mg, 86% yield) as a white solid.

A portion of **546** (16 mg) was re-purified with achiral reverse phase HPLC (XBridge C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/Mobile Phase B: ACN (0.05% TFA), 5 to 95% of Mobile Phase B over 9 min, 100% of Mobile Phase B hold 1 min, flow rate= 25 mL/min) and lyophilized to provide **546** (14 mg, 85% yield). (LC/MS) m/z $(M+H)^+$ = 601.9. ^1H NMR (600 MHz, $(CD_3)_2SO$) δ 8.57 – 8.52 (m, 1H), 8.29 – 8.27 (m, 1H), 8.26 – 8.22 (m, 1H), 7.72 – 7.67 (m, 1H), 7.43 – 7.38 (m, 2H), 7.23 – 7.15 (m, 2H), 6.87 – 6.82 (m, 1H), 4.72 – 4.65 (m, 1H), 4.56 – 4.50 (m, 1H), 4.41 – 4.33 (m, 2H), 4.31 – 4.26 (m, 1H), 4.13 – 4.07 (m, 1H), 3.22 – 3.15 (m, 2H), 2.99 (s, 6H), 2.93 – 2.90 (m, 6H), 1.48 – 1.40 (m, 6H).

Example 547 and 548

rel-(R or S)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(547 and 548)**



Step 1. Separation of *rel-(R or S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(547 and 548)**

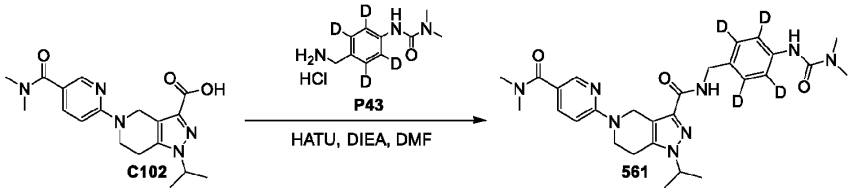
546 (56 mg) was purified with chiral SFC [Column: Chiral Technologies OD-H C_{18} 250 mm x 21 mm x 5 µm, Mobile phase: (3:2) CO_2/MeOH (0.2% NH_4OH), isocratic over 10 min, flow rate= 75 mL/ min; backpressure: 120 bar] and lyophilized to provide the first eluting isomer as **548** (22 mg, 38% yield) and the second eluting isomer as **547** (21 mg, 38% yield). The chiral purity was determined using SFC analytical method on Chiral Technologies OD-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH (0.2% NH_4OH); isocratic gradient: 50% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar to provide

Example **548**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 601.3 at retention time: 1.99 min).and Example **547**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 601.3 at retention time: 3.94 min).

547: (LC/MS) m/z $(M+H)^+$ = 601.3. ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.55 (t, 1H), 8.29 – 8.27 (m, 1H), 8.24 (s, 1H), 7.69 (dd, 1H), 7.42 – 7.38 (m, 2H), 7.21 – 7.17 (m, 2H), 6.84 (d, 1H), 4.72 – 4.65 (m, 1H), 4.57 – 4.49 (m, 1H), 4.42 – 4.32 (m, 2H), 4.31 – 4.25 (m, 1H), 4.16 – 4.06 (m, 1H), 3.30 – 3.27 (m, 1H), 3.18 – 3.15 (m, 1H), 2.99 (s, 6H), 2.91 (s, 6H), 1.44 (dd, 6H).

Example 561

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido) 2,3,5,6-d_4-benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(561)**

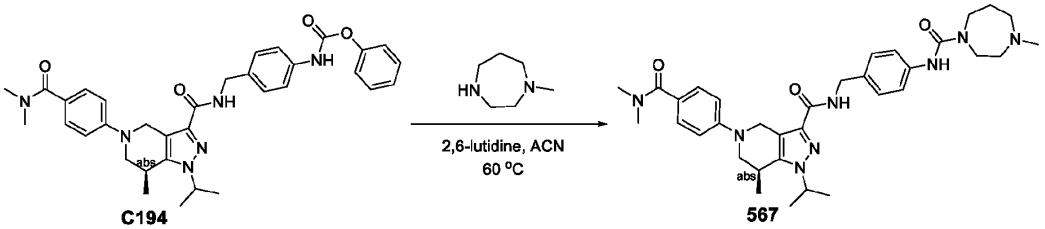


Step 1. Preparation of 5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido) 2,3,5,6-d_4-benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(561)**

To a solution of **C102** (0.940 g, 2.63 mmol) and **P43** (1.05 g, 3.16 mmol) in DMF (10 mL) were added DIEA (1.36 g, 10.5 mmol) and HATU (1.10 g, 2.89 mmol). The reaction mixture was stirred at room temperature for 2 h then poured into H_2O (30 mL) and extracted with EtOAc: THF (2:1, 4 x 30 mL). The combined organic layer was washed with brine (3 x 50 mL) then dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 5% MeOH: DCM). The resultant residue was slurried with MeOH (20 mL) at room temperature for 30 min then filtered. The filter cake was dried *in vacuo* then collected to provide **561** (0.509 g, 34.5% yield) as a white solid. (LC/MS) m/z $(M+H)^+$ = 537.3. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.32 (t, 1H), 8.26 – 8.19 (m, 2H), 7.63 (dd, 1H), 6.88 (d, 1H), 4.75 (s, 2H), 4.55 – 4.43 (m, 1H), 4.35 (d, 2H), 3.95 (t, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.82 (t, 2H), 1.39 (d, 6H).

Example 567

(*S*)-5-(4-(Dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(567)**

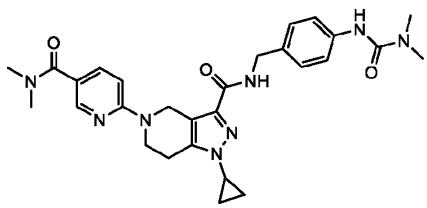


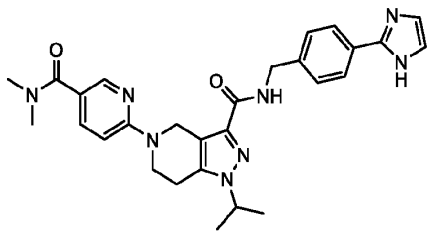
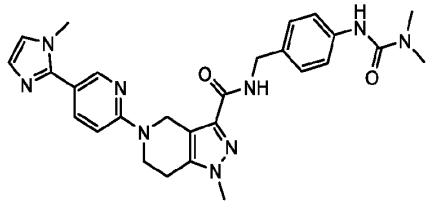
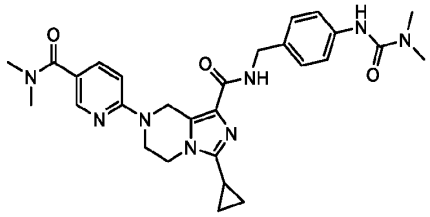
Step 1. Preparation of (*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide **(567)**

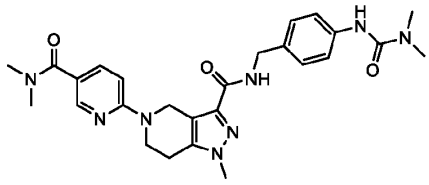
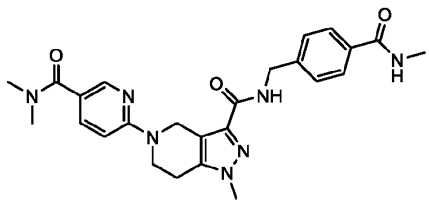
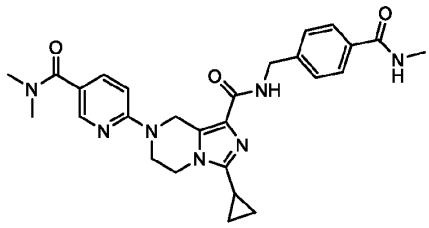
To a reaction mixture of **C194** (0.050 g, 0.079 mmol) and 1-methylhomopiperazine (CAS: 4318-37-0; 18 mg, 0.16 mmol) in ACN (0.8 mL) was added 2,6-lutidine (25 mg, 0.24 mmol). The suspension was stirred at 60 °C for 2 h then concentrated *in vacuo*. The residue was dissolved in DMSO then filtered and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O (0.05% TFA)/Mobile Phase B: ACN (0.05% TFA), 5 to 95% of Mobile Phase B over 10 min, flow rate= 25 mL/min) and lyophilized to provide **567** (37 mg, 76% yield). (LC/MS) m/z $(M+H)^+$ = 615.6.

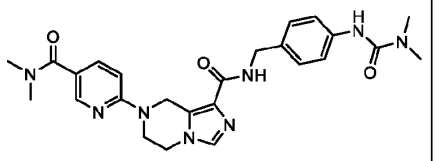
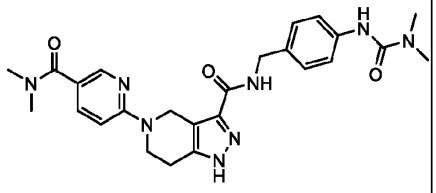
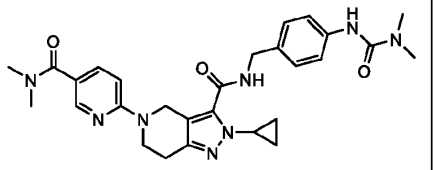
Examples 10-757

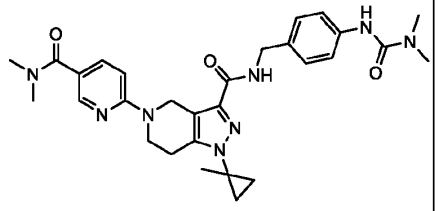
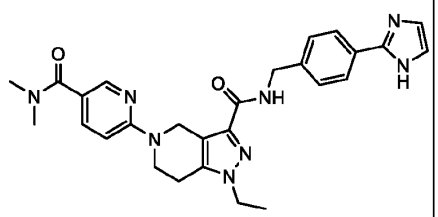
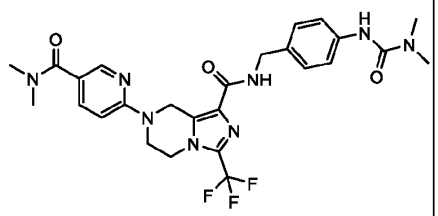
The compounds in Table 1 were prepared using similar chemistry as described above in the selected Examples 1-567 that are commercially available or that can be synthesized by literature methods to form the resultant compounds of the disclosure.

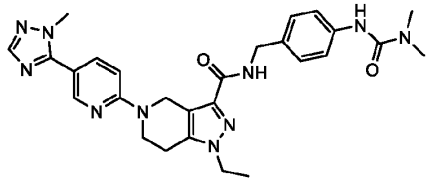
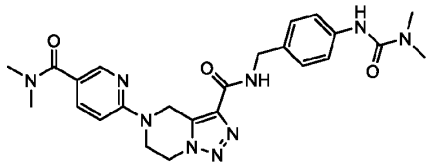
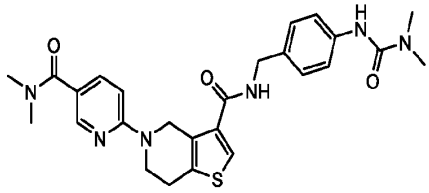
Ex.	Method of Synthesis	Structure	ChemDraw Name	LC/MS m/z $(M+H)^+$/NMR
10	Ex. 10		1-cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	531.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.22-8.21 (m, 2H), 7.68 (dd, 1H), 7.40 – 7.34 (m, 2H), 7.15 (d, 2H), 6.96 (d, 1H), 4.75 (s, 2H), 4.32 (d, 2H), 3.96 (t, 2H), 3.56 (tt, 1H), 2.97 (s, 6H), 2.91-2.86 (m, 8H), 1.12-1.05 (m, 2H), 1.01 – 0.95 (m, 2H).

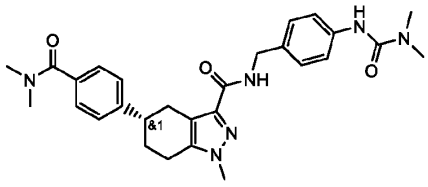
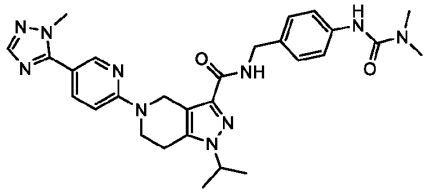
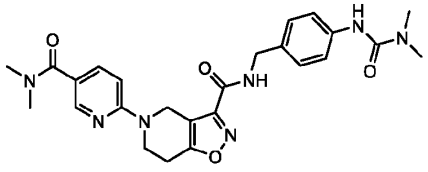
11	Ex. 10		*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	513.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 14.61 (br s, 1H), 8.62 (t, 1H), 8.23 (d, 1H), 7.96 – 7.92 (m, 2H), 7.82 (s, 2H), 7.64 (dd, 1H), 7.57 (d, 2H), 6.89 (d, 1H), 4.74 (s, 2H), 4.56 – 4.48 (m, 3H), 3.95 (t, 2H), 2.99- 2.94 (m, 6H), 2.84 (t, 2H), 1.41 (d, 6H).
12	Ex. 12		*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	514.4; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.43 (d, 1H), 8.22 (s, 1H), 7.84 (dd, 1H), 7.42 – 7.34 (m, 2H), 7.22 (s, 1H), 7.16 (d, 2H), 7.01 – 6.93 (m, 2H), 4.77 (s, 2H), 4.32 (d, 2H), 3.96 (t, 2H), 3.76 (s, 3H), 3.71 (s, 3H), 2.90 (s, 6H), 2.80 (t, 2H).
13	Ex. 5		3-cyclopropyl-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	531.5; ^{1}H NMR (400 MHz, CD_3OD) δ 8.31 (d, 1H), 7.73 (dd, 1H), 7.35 – 7.23 (m, 4H), 6.95 (d, 1H), 5.04 (s, 2H), 4.47 (s, 2H), 4.20 (s, 4H), 3.09 (s, 6H), 3.01 (s, 6H), 1.97– 1.88 (m, 1H), 1.03 – 0.89 (m, 4H).

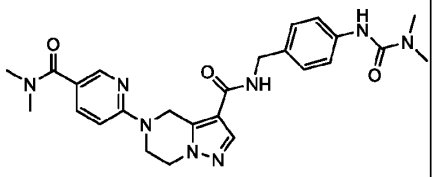
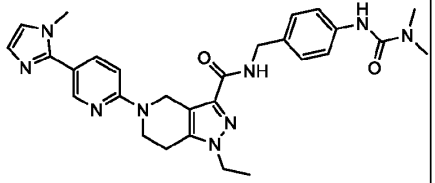
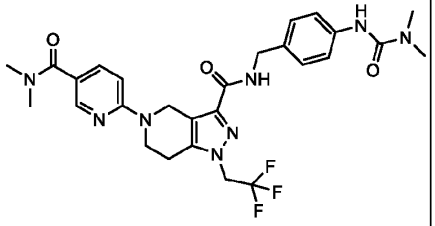
14	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	505.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.48 (t, 1H), 8.25 – 8.18 (m, 2H), 7.66 (dd, 1H), 7.37 (d, 2H), 7.15 (d, 2H), 6.93 (d, 1H), 4.76 (s, 2H), 4.32 (d, 2H), 3.95 (t, 2H), 3.75 (s, 6H), 2.96 (s, 3H), 2.90 (s, 6H), 2.79 (t, 2H).
15	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	476.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.27-8.25 (m, 1H), 7.80 – 7.75 (m, 2H), 7.66 (dd, 1H), 7.44 (d, 2H), 6.89 (d, 1H), 4.77 (s, 2H), 4.59 (s, 2H), 4.07 (t, 2H), 3.80 (s, 3H), 3.08 (s, 6H), 2.91 (s, 3H), 2.83 (t, 2H).
16	Ex. 5		3-cyclopropyl-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(methylcarbamoyl)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	502.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.31 (d, 1H), 7.79 – 7.75 (m, 2H), 7.74- 7.69 (m, 1H), 7.43 (d, 2H), 6.95 (d, 1H), 5.04 (s, 2H), 4.58 (s, 2H), 4.20 (s, 5H), 3.09 (s, 7H), 2.90 (s, 3H), 1.98 – 1.89 (m, 1H), 1.03 – 0.89 (m, 4H).

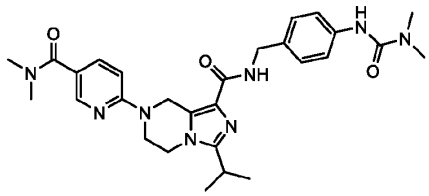
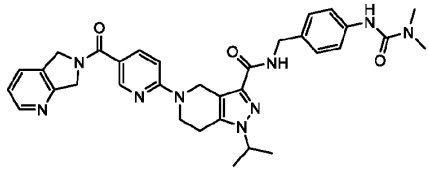
17	Ex. 5		7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	491.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.32-8.29 (m, 1H), 7.72 (dd, 1H), 7.62 (s, 1H), 7.36 – 7.31 (m, 2H), 7.29 - 7.25 (m, 2H), 6.94 (d, 1H), 5.07 (s, 2H), 4.50 (s, 2H), 4.26 – 4.11 (m, 4H), 3.09 (s, 6H), 3.00 (s, 6H).
18	Ex. 18		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	491.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.26 (d, *J* = 2.4 Hz, 1H), 7.67 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.35-7.25 (m, 4H), 6.89 (d, *J*=8.9 Hz, 1H),4.78 (s, 2H), 4.50 (s, 2H), 4.05 (t, *J* = 5.6 Hz, 2H), 3.08 (s, 6H), 3.00 (s, 6H), 2.84 (t, *J* = 5.8 Hz, 2H).
19	Ex.10		2-cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	531.6; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ = 8.69 (t, 1H), 8.29 – 8.21 (m, 2H), 7.68 (dd, 1H), 7.49 – 7.42 (m, 2H), 7.27 – 7.18 (m, 2H), 6.88 (d, 1H), 4.70 (s, 2H), 4.43 (d, 2H), 3.99 – 3.87 (m, 3H), 3.00-2.94 (m, 6H), 2.92 (s, 6H), 2.69 (t, 2H), 1.00-0.92 (m, 2H), 0.91 – 0.86 (m, 2H).

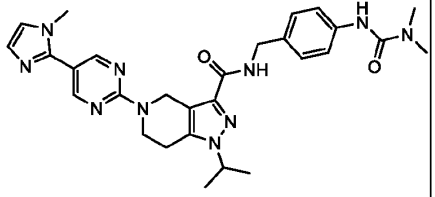
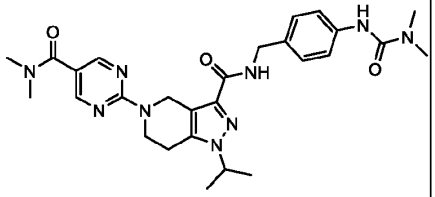
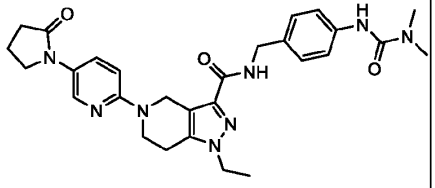
20	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	545.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.26 (d, 1H), 7.67 (dd, 1H), 7.35 – 7.31 (m, 2H), 7.29-7.25 (m, 2H), 6.88 (d, 1H), 4.74 (s, 2H), 4.48 (s, 2H), 4.06 (t, 2H), 3.08 (s, 6H), 3.01-2.99 (m, 6H), 2.94 (t, 2H), 1.51 (s, 3H), 1.24 (t, 2H), 0.96 (t, 2H).
21	Ex. 5		*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	499.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 (d, 1H), 7.87 – 7.81 (m, 2H), 7.67 (dd, 1H), 7.49-7.44 (m, 2H), 7.14 (s, 2H), 6.90 (d, 1H), 4.78 (s, 2H), 4.59 (s, 2H), 4.20 – 4.01 (m, 4H), 3.14- 3.05 (m, 6H), 2.91 – 2.82 (m, 2H), 1.42 (t, 3H).
22	Ex. 5		7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	559.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.32 (d, 1H), 7.74 (dd, 1H), 7.37 – 7.31 (m, 2H), 7.31 – 7.24 (m, 2H), 6.98 (d, 1H), 5.15 (s, 2H), 4.49 (s, 2H), 4.33 (t, 2H), 4.21 (t, 2H), 3.09 (s, 6H), 3.01 (s, 6H).

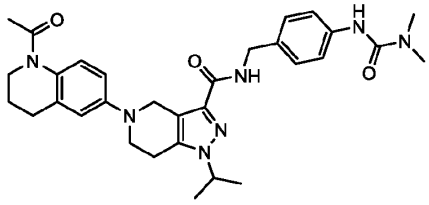
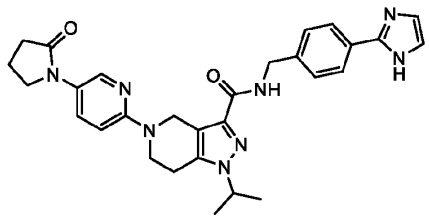
23	Ex. 23		*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxamide	529.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.56 (d, 1H), 8.44 (t, 1H), 8.23 (s, 1H), 7.99 – 7.92 (m, 2H), 7.45 – 7.34 (m, 2H), 7.22 – 7.17 (m, 2H), 7.05 (d, 1H), 4.83 (s, 2H), 4.36 (d, 2H), 4.11 (q, 2H), 4.02 (t, 2H), 3.97 (s, 3H), 2.93 (s, 6H), 2.86 (t, 2H), 1.36 (t, 3H).
24	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-*a*]pyrazine-3-carboxamide	492.3; ^{1}H NMR* (400 MHz, CD_3OD) δ 8.32 (d, 1H), 7.74 (dd, 1H), 7.37 – 7.32 (m, 2H), 7.28-7.25 (m, 2H), 7.00 (d, 1H), 5.12 (s, 2H), 4.57- 4.50 (m, 4H), 4.25 (t, 2H), 3.08 (s, 6H), 3.00 (s, 6H).
25	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine-3-carboxamide	507.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.25 (d, 1H), 7.79 (s, 1H), 7.66 (dd, 1H), 7.36 – 7.30 (m, 2H), 7.30 – 7.23 (m, 2H), 6.86 (d, 1H), 4.83-4.81 (m, 2H), 4.47 (s, 2H), 4.05 (t, 2H), 3.08 (s, 6H), 3.00 (s, 6H), 2.93 (t, 2H).

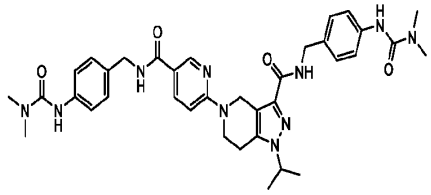
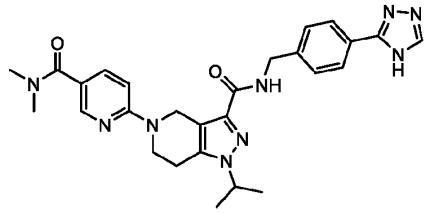
26	Ex. 26		*rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxamide	503.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.31 (t, 1H), 8.22 (s, 1H), 7.41 – 7.34 (m, 6H), 7.19 – 7.10 (m, 2H), 4.31 (d, 2H), 3.76 (s, 3H), 3.13- 3.04 (m, 2H), 2.99-2.87 (m, 12H), 2.86 – 2.57 (m, 4H), 2.13 – 1.89 (m, 2H).
27	Ex. 23		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	543.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.56 (d, 1H), 8.34 (t, 1H), 8.24 (s, 1H), 7.98 – 7.92 (m, 2H), 7.45 – 7.38 (m, 2H), 7.26 – 7.18 (m, 2H), 7.05 (d, 1H), 4.83 (s, 2H), 4.51-4.46 (m, 1H), 4.38 (d, 2H), 4.03 (t, 2H), 3.97 (s, 3H), 2.93 (s, 6H), 2.87 (t, 2H), 1.43 (d, 6H).
28	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydroisoxazolo[4,5-*c*]pyridine-3-carboxamide	492.3; ^{1}H NMR* (400 MHz, CD_3OD) δ 8.26 (d, 1H), 7.67 (dd, 1H), 7.35 – 7.29 (m, 2H), 7.29 – 7.23 (m, 2H), 6.92 (d, 1H), 4.71 (s, 2H), 4.49 (s, 2H), 4.07 (t, 2H), 3.07 (s, 6H), 2.99 (s, 6H), 2.97 – 2.89 (t, 2H).

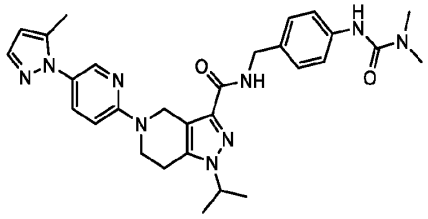
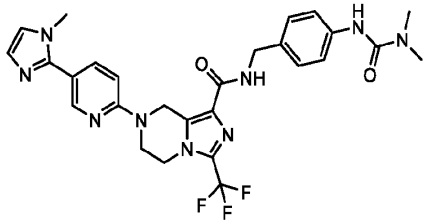
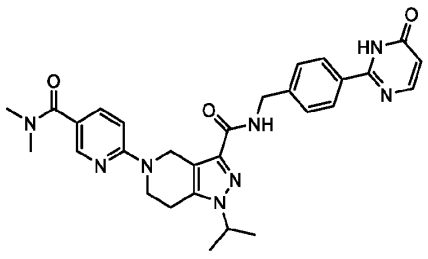
29	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-3-carboxamide	491.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.34-8.31 (m, 1H), 7.96 (s, 1H), 7.74 (dd, 1H), 7.36- 7.32 (m, 2H), 7.29-7.24 (m, 2H), 7.01-6.98 (m, 1H), 5.09 (s, 2H), 4.48 (s, 2H), 4.32 – 4.24 (m, 4H), 3.10 (s, 6H), 3.02 (d, 6H).
30	Ex. 30		*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.37 (d, 1H), 7.80 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.30 – 7.26 (m, 2H), 7.15 (d, 1H), 7.01 (d, 1H), 6.98 (d, 1H), 4.78 (s, 2H), 4.50 (s, 2H), 4.16 – 4.04 (m, 4H), 3.74 (s, 3H), 3.01 (s, 6H), 2.85 (t, 2H), 1.41 (t, 3H).
31	Ex. 18		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.52 (t, 1H), 8.24 – 8.21 (m, 2H), 7.66 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.18- 7.15 (m, 2H), 6.94 (d, 1H), 5.13 (q, 2H), 4.77 (s, 2H), 4.34 (d, 2H), 3.96 (t, 2H), 2.97 (s, 6H), 2.90 (s, 6H), 2.84 (t, 2H).

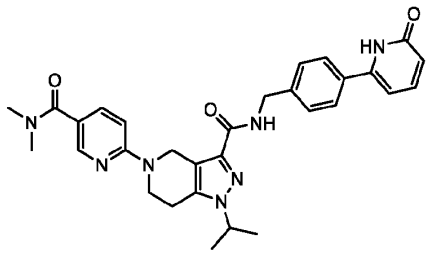
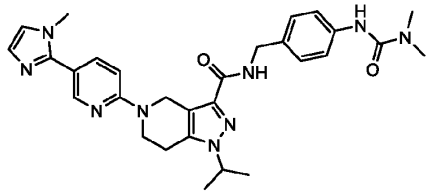
32	Ex. 5		7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	533.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.30-8.28 (m, 1H), 7.71 (dd, 1H), 7.35-7.31 (m, 2H), 7.28 – 7.24 (m, 2H), 6.93 (d, 1H), 5.04 (s, 2H), 4.48 (s, 2H), 4.19 – 4.08 (m, 4H), 3.17-3.04 (m, 7H), 2.99 (s, 6H), 1.28 (d, 6H).
33	Ex. 5		5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	608.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.54 – 8.44 (m, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.94 – 7.67 (m, 2H), 7.42 – 7.37 (m, 2H), 7.32 (br s, 1H), 7.21 – 7.16 (m, 2H), 6.94 (d, 1H), 5.01 – 4.88 (m, 3H), 4.84 – 4.72 (m, 3H), 4.56 – 4.45 (m, 1H), 4.36 (d, 2H), 3.99 (t, 2H), 2.91 (s, 6H), 2.85 (t, 2H), 1.41 (d, 6H).

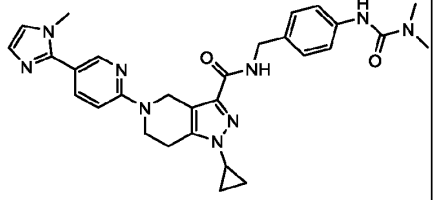
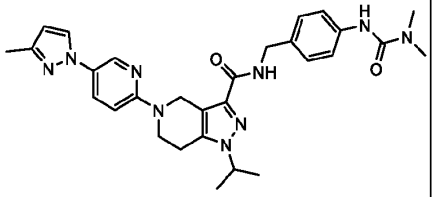
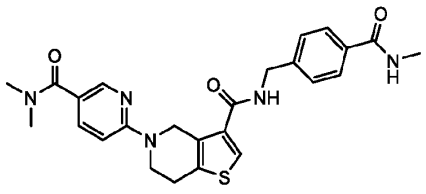
34	Ex. 34		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	543.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.69 (s, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.42 – 7.36 (m, 2H), 7.24 (d, 1H), 7.19 – 7.13 (m, 2H), 6.95 (d, 1H), 4.96 (s, 2H), 4.53-4.43 (m, 1H), 4.34 (d, 2H), 4.14 (t, 2H), 3.71 (s, 3H), 2.90 (s, 6H), 2.83 (t, 2H), 1.39 (d, 6H).
35	Ex. 35		5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	534.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.51 (s, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.41 – 7.35 (m, 2H), 7.16 (d, 2H), 4.94 (s, 2H), 4.52 – 4.42 (m, 1H), 4.33 (d, 2H), 4.12 (t, 2H), 2.97 (br s, 6H), 2.90 (s, 6H), 2.81 (t, 2H), 1.38 (d, 6H).
36	Ex. 36		*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	531.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.42 (t, 1H), 8.30 (d, 1H), 8.23 (s, 1H), 7.90 (dd, 1H), 7.43 – 7.36 (m, 2H), 7.18 (d, 2H), 6.92 (d, 1H), 4.67 (s, 2H), 4.34 (d, 2H), 4.08 (q, 2H), 3.88 (t, 2H), 3.78 (t, 2H), 2.92 (s, 6H), 2.80 (t, 2H), 2.44 (t, 2H), 2.14 – 2.01 (m, 2H), 1.33 (t, 3H).

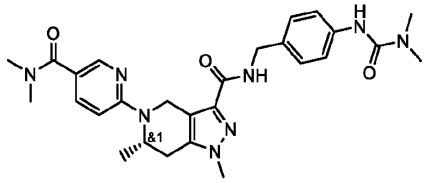
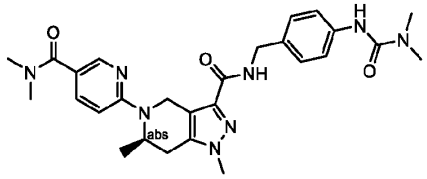
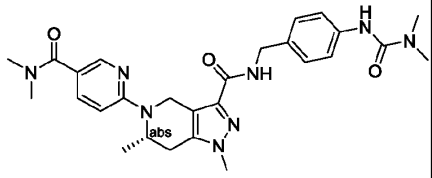
37	Ex. 37		5-(1-acetyl-1,2,3,4-tetrahydroquinolin-6-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	558.5; ^{1}H NMR (400 MHz, CD_3OD) δ 7.36 – 7.31 (m, 2H), 7.30 – 7.25 (m, 2H), 7.08 (br s, 1H), 6.90 (d, 2H), 4.54 – 4.46 (m, 3H), 4.40 (s, 2H), 3.73 (t, 2H), 3.61 (t, 2H), 3.00 (s, 6H), 2.85 (t, 2H), 2.72-2.63 (m, 2H), 2.16 (br s, 3H), 1.92 (br s, 2H), 1.46 (d, 6H).
38	Ex. 1		*N*-(4-(1*H*-imidazol-2-yl)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	525.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.44 (br s, 1H), 8.47 (t, 1H), 8.30 (d, 1H), 7.93 – 7.85 (m, 3H), 7.38 (d, 2H), 7.22 (br s, 1H), 7.00 (br s, 1H), 6.91 (d, 1H), 4.66 (s, 2H), 4.56 – 4.41 (m, 3H), 3.88 (t, 2H), 3.77 (t, 2H), 2.82 (t, 2H), 2.44 (t, 2H), 2.14 – 1.99 (m, 2H), 1.41 (d, 6H).

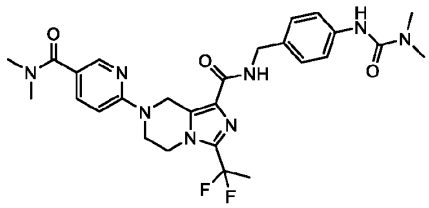
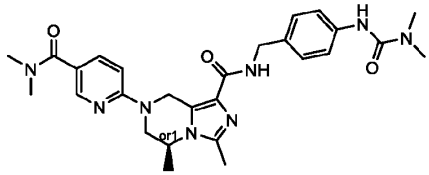
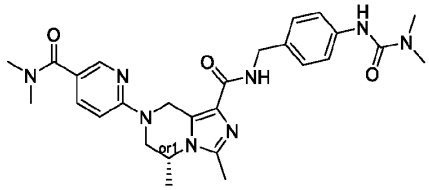
39	Ex. 39		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	681.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.75 (t, 1H), 8.65 (d, 1H), 8.34 (t, 1H), 8.23 (d, 2H), 8.01 (dd, 1H), 7.41 – 7.35 (m, 4H), 7.20- 7.12 (m, 4H), 6.90 (d, 1H), 4.76 (s, 2H), 4.54 – 4.42 (m, 1H), 4.35 (dd, 4H), 3.97 (t, 2H), 2.81 (t, 2H), 1.39 (d, 6H).
40	Ex 5		*N*-(4-(4*H*-1,2,4-triazol-3-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	514.3; ^{1}H NMR* (400 MHz, CD_3OD) δ 8.61-8.47 (m, 1H), 8.31- 8.25 (m, 1H), 8.04-7.90 (m, 2H), 7.67 (dd, 1H), 7.54- 7.43 (m, 2H), 6.89 (d, 1H), 4.78 (s, 2H), 4.64- 4.59 (m, 2H), 4.57- 4.49 (m, 1H), 4.08 (t, 2H), 3.08 (s, 6H), 2.87 (t, 2H), 1.52-1.45 (m, 6H).

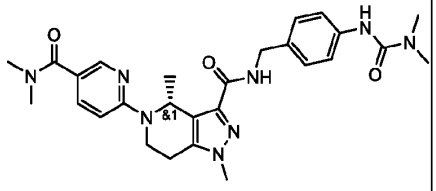
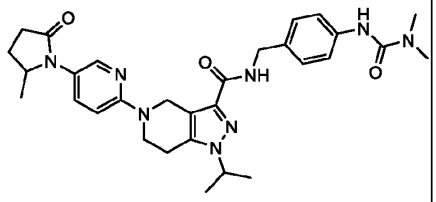
41	Ex. 41		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	542.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, 1H), 7.58- 7.53 (m, 2H), 7.36 (d, 2H), 7.30 (d, 2H), 7.15 (t, 1H), 6.86 (d, 1H), 6.31 (s, 1H), 6.17 (s, 1H), 4.76 (s, 2H), 4.56 (d, 2H), 4.43 – 4.34 (m, 1H), 4.15 (t, 2H), 3.03 (s, 6H), 2.82 (t, 2H), 2.29 (s, 3H), 1.45 (d, 6H).
42	Ex. 42		*N*-(4-(3,3-dimethylureido)benzyl)-7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	568.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.43 (d, 1H), 7.86 (dd, 1H), 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 2H), 7.16 (d, 1H), 7.07 – 7.00 (m, 2H), 5.15 (s, 2H), 4.49 (s, 2H), 4.34 (t, 2H), 4.21 (t, 2H), 3.74 (s, 3H), 3.00 (s, 6H).
43	Ex. 43		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(6-oxo-1,6-dihydropyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	541.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.57 (t, 1H), 8.23 (d, 1H), 8.09 – 8.02 (m, 3H), 7.63 (dd, 1H), 7.43 (d, 2H), 6.88 (d, 1H), 6.29 (d, 1H), 4.74 (s, 2H), 4.57 – 4.41 (m, 3H), 3.95 (t, 2H), 2.96 (s, 6H), 2.82 (t, 2H), 1.40 (d, 6H).

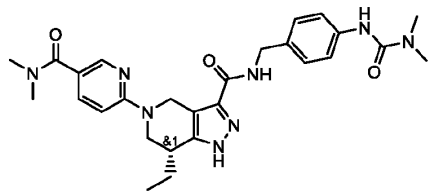
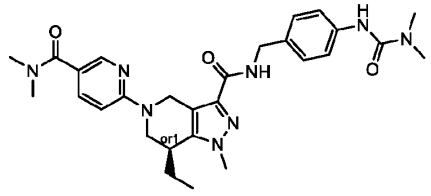
44	Ex 43		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(6-oxo-1,6-dihydropyridin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	540.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 11.54 (br s, 1H), 8.53 (q, 1H), 8.24 – 8.19 (m, 1H), 7.74 – 7.66 (m, 2H), 7.65 – 7.58 (m, 1H), 7.50 (q, 1H), 7.42 – 7.35 (m, 2H), 6.87 (t, 1H), 6.64 – 6.56 (m, 1H), 6.34 (t, 1H), 4.77 – 4.69 (m, 2H), 4.55 – 4.40 (m, 3H), 3.98 – 3.89 (m, 2H), 3.00 – 2.89 (m, 6H), 2.84 – 2.76 (m, 2H), 1.42 - 1.35 (m, 6H).
45	Ex. 45		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	542.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.44 (d, 1H), 8.34 (t, 1H), 8.23 (s, 1H), 7.86 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.24 (br s, 1H), 7.20 – 7.16 (m, 2H), 6.98 (d, 2H), 4.77 (s, 2H), 4.55 – 4.47 (m, 1H), 4.35 (d, 2H), 3.97 (t, 2H), 3.72 (s, 3H) 2.91 (s, 6H), 2.85 (t, 2H), 1.41 (d, 6H).

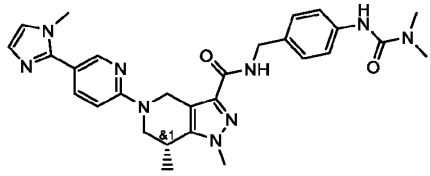
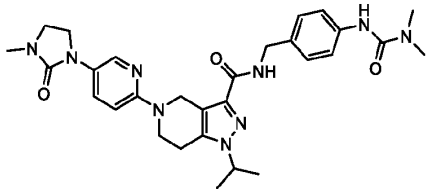
46	Ex. 12		1-cyclopropyl-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	540.5
47	Ex. 1		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	542.4
48	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine-3-carboxamide	478.2; ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 (d, 1H), 7.85 (s, 1H), 7.82 – 7.78 (m, 2H), 7.67 (dd, 1H), 7.46 (d, 2H), 6.88 (d, 1H), 4.86 – 4.84 (m, 2H), 4.59 (s, 2H), 4.05 (t, 2H), 3.09 (s, 6H), 2.95 (t, 2H), 2.91 (s, 3H).

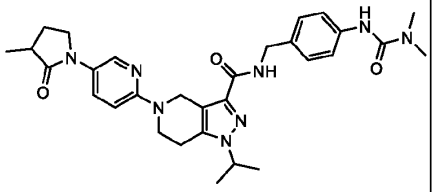
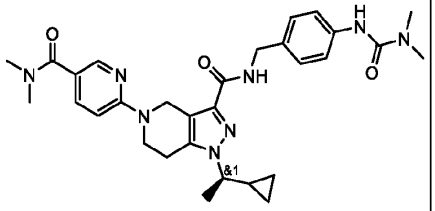
49	Ex. 6		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.32 (m, 1H), 7.63 (d, 1H), 7.35 (d, 2H), 7.28 (d, 2H), 7.10 (t, 1H), 6.74 (d, 1H), 6.34 (s, 1H), 5.73 – 5.63 (m, 1H), 4.97 (d, 1H), 4.61 – 4.49 (m, 2H), 4.33 (d, 1H), 3.75 (s, 3H), 3.08 (s, 6H), 3.04 – 2.98 (m, 7H), 2.54 (d, 1H), 1.13 (d, 3H).
50^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.50 (t, 1H), 8.28 – 8.20 (m, 2H), 7.65 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.20 – 7.13 (m, 2H), 6.85 (d, 1H), 5.33 – 5.09 (m, 2H), 4.38 – 4.25 (m, 2H), 4.08 (d, 1H), 3.82 – 3.71 (m, 3H), 3.02 – 2.95 (m, 6H), 2.93 – 2.86 (m, 7H), 2.78 – 2.65 (m, 1H), 1.07 (d, 3H).
51^	Ex. 113		*(S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.54 – 8.48 (m, 1H), 8.28 – 8.21 (m, 2H), 7.66 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.20 – 7.14 (m, 2H), 6.86 (d, 1H), 5.31 – 5.10 (m, 2H), 4.33 (d, 2H), 4.09 (d, 1H), 3.78 (s, 3H), 3.01 – 2.95 (m, 6H), 2.94 – 2.88 (m, 7H), 2.77 – 2.69 (m, 1H), 1.07 (d, 3H).

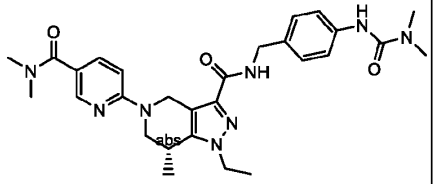
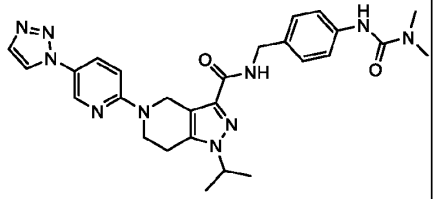
52	Ex. 5		3-(1,1-difluoroethyl)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	555.5; ^{1}H NMR (400 MHz, CD_3OD) δ 8.30 (d, 1H), 7.71 (dd, 1H), 7.34 – 7.28 (m, 2H), 7.26 – 7.21 (m, 2H), 6.94 (d, 1H), 5.10 (s, 2H), 4.47 (s, 2H), 4.38 – 4.29 (m, 2H), 4.21 – 4.12 (m, 2H), 3.07 (s, 6H), 2.98 (s, 6H), 2.17 – 2.01 (m, 3H).
53^	Ex. 5		*rel-(R* or *S)*-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	519.5; 1H NMR (400 MHz, CD_3OD) δ 8.31 (d, 1H), 7.74 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.28 – 7.24 (m, 2H), 6.94 (d, 1H), 5.39 (d, 1H), 4.85 – 4.80 (m, 1H), 4.58 – 4.53 (m, 2H), 4.49 (s, 2H), 3.50 – 3.31 (m, 1H), 3.10 (s, 6H), 3.00 (s, 6H), 2.41 (s, 3H), 1.40 (d, 3H).
54^	Ex. 5		*rel-(R* or *S)*-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	519.5; 1H NMR (400 MHz, CD_3OD) δ 8.31 (d, 1H), 7.74 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.28 – 7.24 (m, 2H), 6.94 (d, 1H), 5.39 (d, 1H), 4.85 – 4.80 (m, 1H), 4.58 – 4.53 (m, 2H), 4.49 (s, 2H), 3.50 – 3.31 (m, 1H), 3.10 (s, 6H), 3.00 (s, 6H), 2.41 (s, 3H), 1.40 (d, 3H).

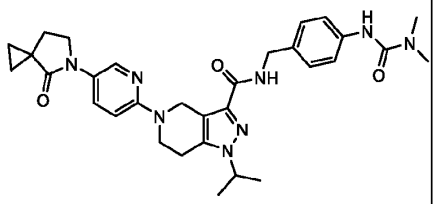
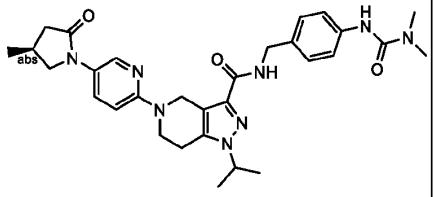
55	Ex. 113		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,4-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.5
56	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-5-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.4

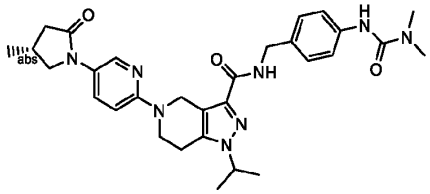
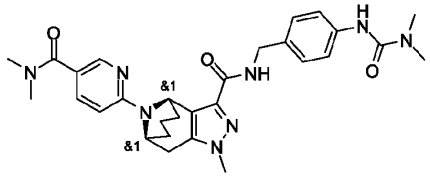
57	Ex. 43		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 13.07 (s, 1H), 8.58 – 8.50 (m, 1H), 8.25 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.19 – 7.14 (m, 2H), 6.85 (d, 1H), 4.80 – 4.58 (m, 2H), 4.42 – 4.25 (m, 2H), 4.04 – 3.89 (m, 1H), 3.81 – 3.67 (m, 1H), 2.97 (s, 6H), 2.93 – 2.88 (m, 7H), 1.85 – 1.70 (m, 1H), 1.60 – 1.46 (m, 1H), 1.00 (t, 3H).
58^	Ex. 58		*rel*-(*R or S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (t, 1H), 8.27 – 8.21 (m, 2H), 7.65 (dd, 1H), 7.40 – 7.34 (m, 2H), 7.18 – 7.11 (m, 2H), 6.83 (d, 1H), 5.00 (d, 1H), 4.76 – 4.69 (m, 1H), 4.42 – 4.16 (m, 3H), 3.81 (s, 3H), 3.24 – 3.15 (m, 1H), 3.02 – 2.93 (m, 7H), 2.92 – 2.87 (m, 6H), 1.66 – 1.53 (m, 1H), 1.50 – 1.36 (m, 1H), 1.02 (t, 3H).

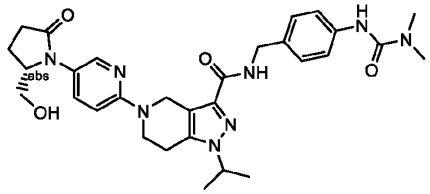
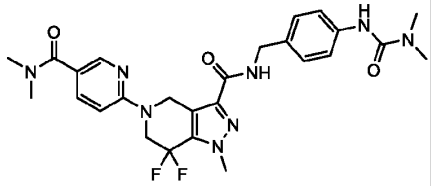
59	Ex. 42		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.5; 1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.50 (t, 1H), 8.43 (d, 1H), 8.23 (s, 1H), 7.84 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.22 – 7.13 (m, 3H), 7.00 – 6.91 (m, 2H), 5.03 (d, 1H), 4.41 – 4.22 (m, 4H), 3.83 (s, 3H), 3.71 (s, 3H), 3.50 – 3.39 (m, 1H), 3.25 – 3.17 (m, 1H), 2.90 (s, 6H), 1.23 (d, 3H).
60	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	560.4

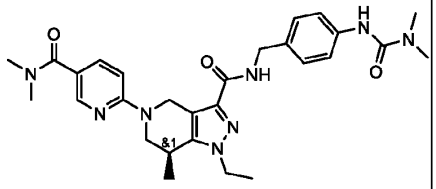
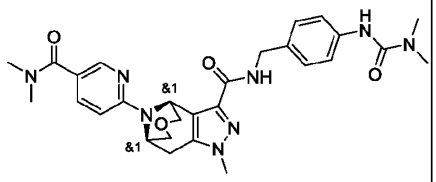
61	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.4
62	Ex. 5		*rac*-(*R*)-1-(1-cyclopropylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.25 (d, 1H), 7.66 (dd, 1H), 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 2H), 6.88 (d, 1H), 4.81 – 4.68 (m, 2H), 4.49 (s, 2H), 4.17 – 3.94 (m, 2H), 3.67 – 3.56 (m, 1H), 3.14 – 3.03 (s, 6H), 2.99 (s, 6H), 2.81 (t, 2H), 1.55 (d, 3H), 1.44 – 1.32 (m, 1H), 0.69 – 0.57 (m, 1H), 0.49 – 0.37 (m, 1H), 0.35 – 0.20 (m, 2H).

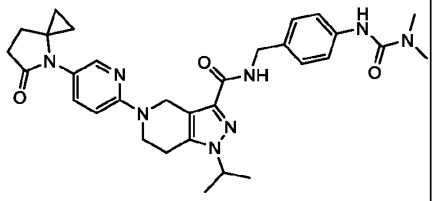
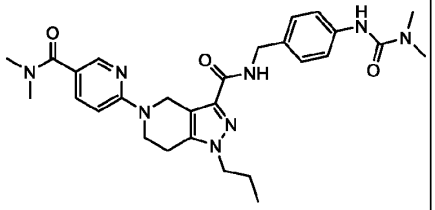
63^	Ex.1[a]		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 – 8.26 (m, 1H), 7.68 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.23 (m, 2H), 6.89 (d, 1H), 5.04 (d, 1H), 4.64 – 4.56 (m, 1H), 4.49 (s, 2H), 4.36 (d, 1H), 4.14 (q, 2H), 3.43 – 3.32 (m, 1H), 3.26 – 3.15 (m, 1H), 3.09 (s, 6H), 3.00 (s, 6H), 1.46 (t, 3H), 1.28 (d, 3H).
64	Ex. 19		5-(5-(1*H*-1,2,3-triazol-1-yl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	529.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.68 – 8.65 (m, 1H), 8.59 (d, 1H), 8.36 (t, 1H), 8.24 (s, 1H), 8.01 (dd, 1H), 7.95 – 7.91 (m, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 7.08 (d, 1H), 4.77 (s, 2H), 4.56 – 4.43 (m, 1H), 4.35 (d, 2H), 3.97 (t, 2H), 2.90 (s, 6H), 2.88 – 2.80 (m, 2H), 1.39 (d, 6H).

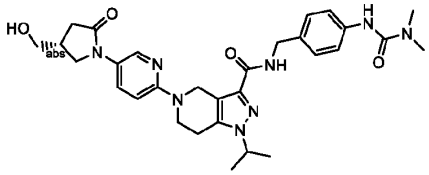
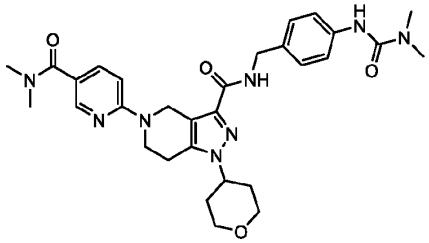
65	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-oxo-5-azaspiro[2.4]heptan-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	571.4
66	Ex. 1[a]		*(S)*-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methyl-2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.4

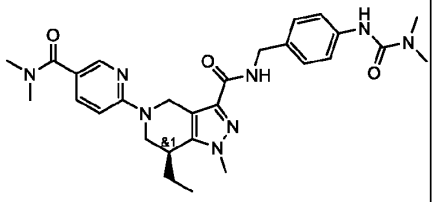
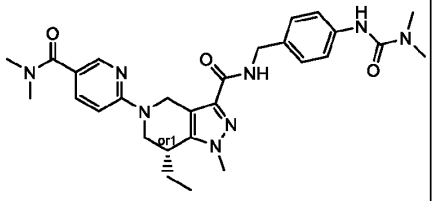
67	Ex. 1[a]		*(R)-N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methyl-2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.4
68	Ex.5		*rac*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxamide	545.3; ^{1}H NMR* (400 MHz, CD_3OD) δ 8.38 – 8.31 (m, 1H), 8.24 (d, 1H), 7.61 (dd, 1H), 7.37 – 7.31 (m, 2H), 7.30 – 7.24 (m, 2H), 6.87 (d, 1H), 5.90 – 5.83 (m, 1H), 5.26 – 5.16 (m, 1H), 4.49 (d, 2H), 3.75 (s, 3H), 3.17 – 3.03 (m, 7H), 3.01 (s, 6H), 2.65 (d, 1H), 1.97 – 1.78 (m, 4H), 1.59 – 1.42 (m, 2H).

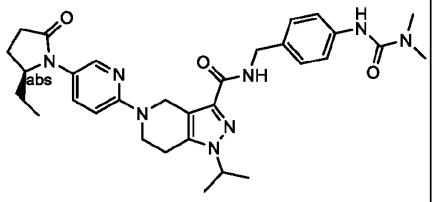
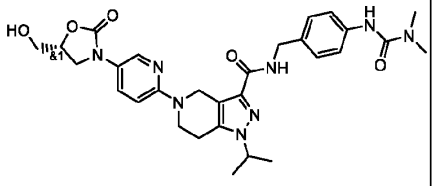
69	Ex. 1[a]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-(hydroxymethyl)-5-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4
70	Ex. 87		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7,7-difluoro-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	541.2; ^{1}H NMR (400 MHz, CD_3OD) δ 8.30 (d, 1H), 7.72 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.24 (m, 2H), 6.99 (d, 1H), 4.62 – 4.57 (m, 2H), 4.52 – 4.42 (m, 4H), 4.04 (s, 3H), 3.12 – 3.03 (m, 6H), 3.01 – 2.95 (m, 6H).

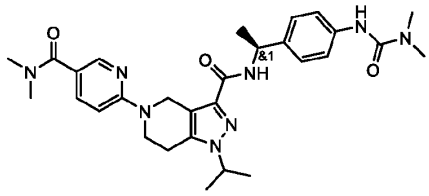
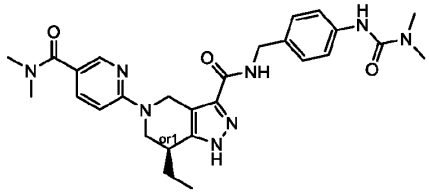
71	Ex. 43		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.27 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.40 – 7.35 (m, 2H), 7.19 – 7.14 (m, 2H), 6.89 (d, 1H), 5.05 (d, 1H), 4.41 – 4.23 (m, 4H), 4.19 – 4.04 (m, 2H), 3.28 – 3.16 (m, 2H), 2.98 (s, 6H), 2.93 – 2.87 (m, 6H), 1.38 (t, 3H), 1.20 (d, 3H).
72	Ex. 87		*rac*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-1,4,5,7,8,9-hexahydro-4,8-epiminooxocino[5,4-*c*]pyrazole-3-carboxamide	547.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.25 – 8.18 (m, 2H), 7.63 (dd, 1H), 7.40 – 7.36 (m, 2H), 7.18 – 7.12 (m, 2H), 6.83 (d, 1H), 5.73 (s, 1H), 4.80 – 4.71 (m, 1H), 4.42 – 4.22 (m, 2H), 3.98 – 3.92 (m, 1H), 3.83 – 3.64 (m, 6H), 3.11 – 3.01 (m, 1H), 2.94 (s, 6H), 2.91 (s, 6H), 2.84 – 2.75 (m, 1H).

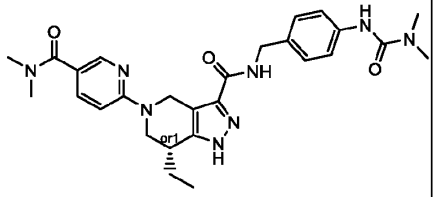
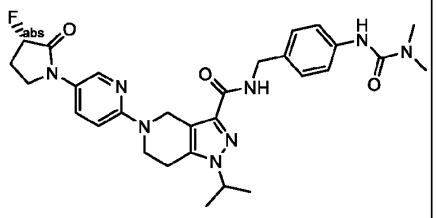
73	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-oxo-4-azaspiro[2.4]heptan-4-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	571.5
74	Ex.5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-propyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.2; ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 – 8.24 (m, 1H), 7.69 – 7.64 (m, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.24 (m, 2H), 6.92 – 6.86 (m, 1H), 4.76 (s, 2H), 4.48 (s, 2H), 4.09 – 4.00 (m, 4H), 3.08 (s, 6H), 3.01 – 2.99 (m, 6H), 2.86 – 2.79 (m, 2H), 1.89 – 1.78 (m, 2H), 0.92 – 0.85 (m, 3H).

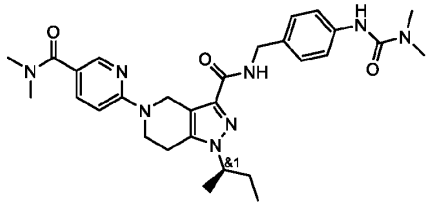
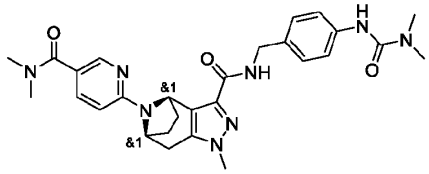
75	Ex. 1[a]		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-(hydroxymethyl)-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4
76	Ex. 5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.42 (t, 1H), 8.25 – 8.22 (m, 2H), 7.64 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.20 – 7.13 (m, 2H), 6.89 (d, 1H), 4.75 (s, 2H), 4.46 – 4.30 (m, 3H), 4.00 – 3.90 (m, 4H), 3.45 (t, 2H), 2.97 (s, 6H), 2.90 (s, 6H), 2.87 – 2.81 (m, 2H), 2.13 – 1.98 (m, 2H), 1.86 – 1.78 (m, 2H).

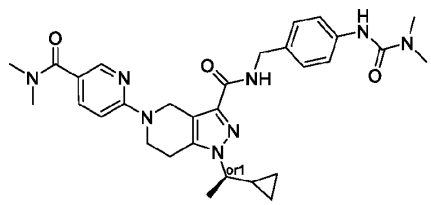
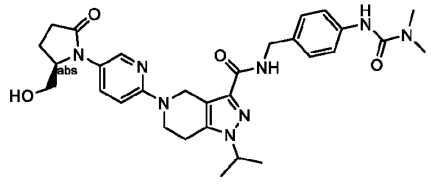
77	Ex. 77		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.51 (t, 1H), 8.27 – 8.20 (m, 2H), 7.65 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.18 – 7.12 (m, 2H), 6.83 (d, 1H), 5.01 (d, 1H), 4.73 (d, 1H), 4.40 – 4.18 (m, 3H), 3.82 (s, 3H), 3.23 – 3.09 (m, 1H), 3.04 – 2.94 (m, 7H), 2.93 – 2.87 (m, 6H), 1.66 – 1.53 (m, 1H), 1.49 – 1.36 (m, 1H), 1.03 (t, 3H).
78^	Ex. 78		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.49 (t, 1H), 8.24 – 8.16 (m, 2H), 7.61 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.16 – 7.09 (m, 2H), 6.80 (d, 1H), 4.97 (d, 1H), 4.69 (d, 1H), 4.35 – 4.15 (m, 3H), 3.78 (s, 3H), 3.20 – 3.10 (m, 1H), 2.98 – 2.91 (m, 7H), 2.87 (m, 6H), 1.62 – 1.49 (m, 1H), 1.46 – 1.32 (m, 1H), 0.99 (t, 3H).

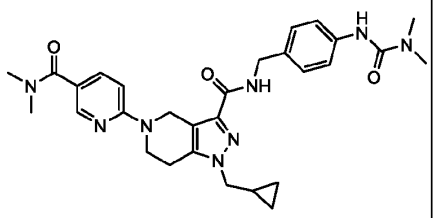
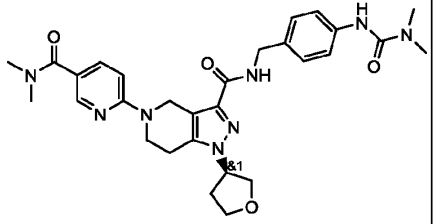
79	Ex. 1[a]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-ethyl-5-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.4
80	Ex. 1[a]		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(5-(hydroxymethyl)-2-oxooxazolidin-3-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	577.4

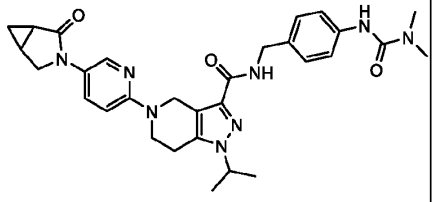
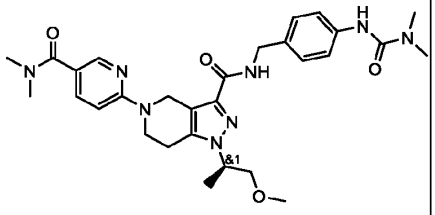
81	Ex. 105		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(1-(4-(3,3-dimethylureido)phenyl)ethyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.26 – 8.20 (m, 2H), 7.99 (d, 1H), 7.62 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.28 – 7.21 (m, 2H), 6.87 (d, 1H), 5.14 – 5.02 (m, 1H), 4.71 (s, 2H), 4.55 – 4.42 (m, 1H), 3.92 (d, 2H), 2.96 (s, 6H), 2.90 (s, 6H), 2.81 (t, 2H), 1.47 (d, 3H), 1.40 (dd, 6H).
82^	Ex. 113		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 13.07 – 13.02 (m, 1H), 8.57 – 8.48 (m, 1H), 8.23 – 8.16 (m, 2H), 7.61 (dd, 1H), 7.38 – 7.30 (m, 2H), 7.16 – 7.10 (m, 2H), 6.82 (d, 1H), 4.75 – 4.56 (m, 2H), 4.38 – 4.25 (m, 2H), 3.96 – 3.89 (m, 1H), 3.79 – 3.70 (m, 1H), 2.99 – 2.90 (m, 6H), 2.89 – 2.82 (m, 7H), 1.82 – 1.69 (m, 1H), 1.58 – 1.43 (m, 1H), 0.97 (t, 3H).

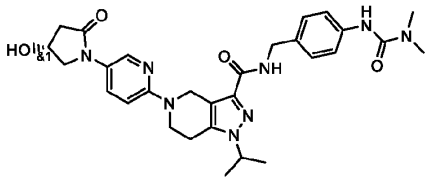
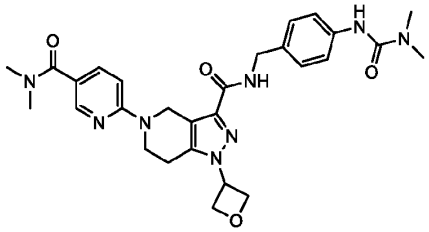
83^	Ex. 113		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 13.04 (s, 1H), 8.56 – 8.49 (m, 1H), 8.24 – 8.16 (m, 2H), 7.60 (dd, 1H), 7.39 – 7.31 (m, 2H), 7.16 – 7.09 (m, 2H), 6.81 (d, 1H), 4.78 – 4.54 (m, 2H), 4.40 – 4.24 (m, 2H), 3.97 – 3.86 (m, 1H), 3.80 – 3.67 (m, 1H), 2.98 – 2.91 (m, 6H), 2.89 – 2.83 (m, 7H), 1.82 – 1.69 (m, 1H), 1.57 – 1.41 (m, 1H), 0.96 (t, 3H).
84	Ex. 1[a]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-fluoro-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	563.3

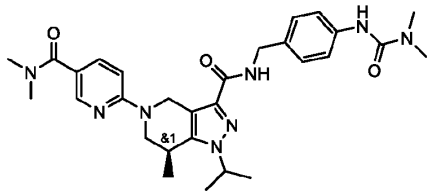
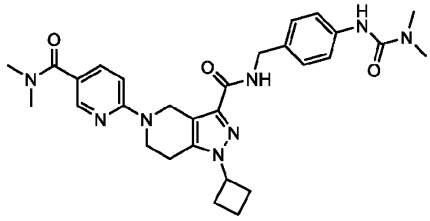
85	Ex. 43		*rac*-(*R*)-1-(*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.26 – 8.19 (m, 2H), 7.63 (dd, 1H), 7.42 – 7.34 (m, 2H), 7.21 – 7.14 (m, 2H), 6.88 (d, 1H), 4.80 – 4.68 (m, 2H), 4.41 – 2.26 (m, 2H), 4.25 – 4.15 (m, 1H), 4.03 – 3.84 (m, 2H), 2.96 (s, 6H), 2.90 (s, 6H), 2.83 – 2.75 (m, 2H), 1.93 – 1.63 (m, 2H), 1.38 (d, 3H), 0.69 (t, 3H).
86	Ex. 5		*rac*-(4*R*,7*S*)-9-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-1,4,5,6,7,8-hexahydro-4,7-epiminocycloheptā[*c*]pyrazole-3-carboxamide	531.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, 1H), 7.39 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 7.06 – 6.99 (m, 1H), 6.61 – 6.53 (m, 2H), 6.31 (s, 1H), 5.55 – 5.52 (m, 1H), 5.10 – 5.00 (m, 1H), 4.62 – 4.44 (m, 2H), 3.59 (s, 3H), 3.32 – 3.19 (m, 1H), 3.06 (s, 3H), 3.03 (s, 6H), 2.85 (s, 3H), 2.46 – 2.27 (m, 3H), 2.14 – 2.03 (m, 1H), 1.72 – 1.63 (m, 1H).

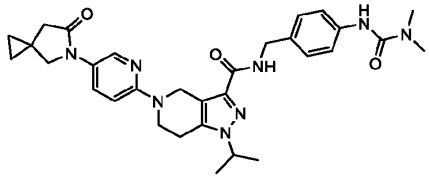
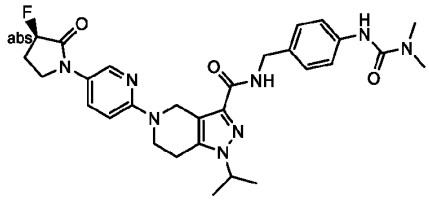
87^	Ex. 5		*rel-(R* or *S)*-1-(1-cyclopropylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 (d, 1H), 7.69 (dd, 1H), 7.39 – 7.33 (m, 2H), 7.32 – 7.28 (m, 2H), 6.91 (d, 1H), 4.86 – 4.71 (m, 2H), 4.52 (s, 2H), 4.22 – 3.96 (m, 2H), 3.71 – 3.58 (m, 1H), 3.10 (s, 6H), 3.02 (s, 6H), 2.84 (t, 2H), 1.58 (d, 3H), 1.46 – 1.35 (m, 1H), 0.72 – 0.61 (m, 1H), 0.52 – 0.42 (m, 1H), 0.39 – 0.25 (m, 2H).
88	Ex. 1[a]		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-(hydroxymethyl)-5-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4

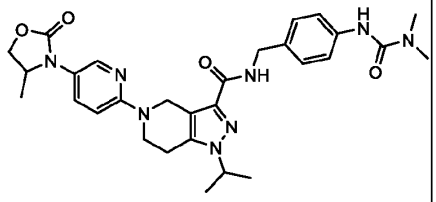
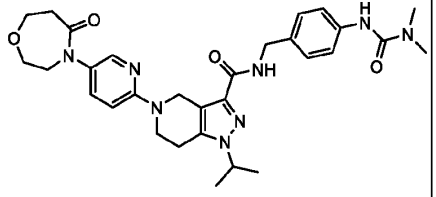
89	Ex. 5		1-(cyclopropylmethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	545.4; ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 – 8.25 (m, 1H), 7.67 (dd, 1H), 7.36 – 7.30 (m, 2H), 7.29 – 7.24 (m, 2H), 6.89 (d, 1H), 4.79 – 4.72 (m, 2H), 4.51 – 4.45 (m, 2H), 4.06 (t, 2H), 3.96 (d, 2H), 3.08 (s, 6H), 3.00 (s, 6H), 2.85 (t, 2H), 1.30 – 1.18 (m, 1H), 0.59 – 0.50 (m, 2H), 0.40 – 0.33 (m, 2H).
90	Ex. 5		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydrofuran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.63 (t, 1H), 8.27 (d, 1H), 7.68 (dd, 1H), 7.37 – 7.31 (m, 2H), 7.30 – 7.25 (m, 2H), 6.90 (d, 1H), 5.07 – 4.97 (m, 1H), 4.78 (s, 2H), 4.52 – 4.48 (m, 1H), 4.20 – 4.00 (m, 5H), 3.93 – 3.85 (m, 1H), 3.09 (s, 6H), 3.01 (s, 6H), 2.88 (t, 2H), 2.50 – 2.37 (m, 1H), 2.34 – 2.23 (m, 1H).

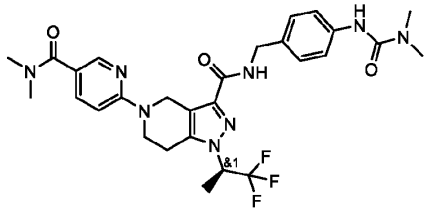
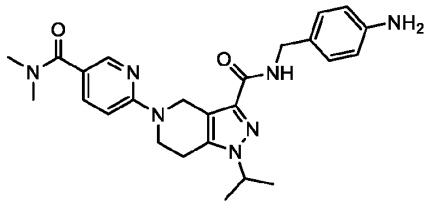
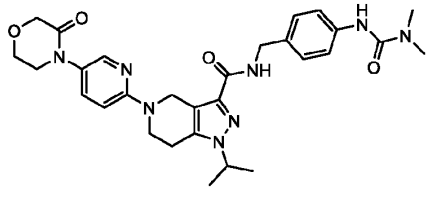
91	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	557.4
92	Ex. 43		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-methoxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	563.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.25 – 8.22 (m, 2H), 7.64 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 6.88 (d, 1H), 4.87 – 4.63 (m, 2H), 4.55 – 4.44 (m, 1H), 4.34 (d, 2H), 4.06 – 3.83 (m, 2H), 3.70 – 3.47 (m, 2H), 3.16 (s, 3H), 2.97 (s, 6H), 2.92 – 2.66 (m, 8H), 1.37 (d, 3H).

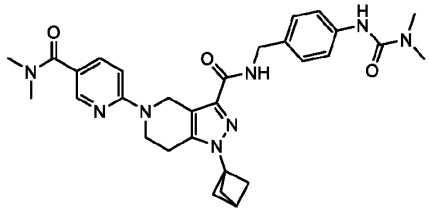
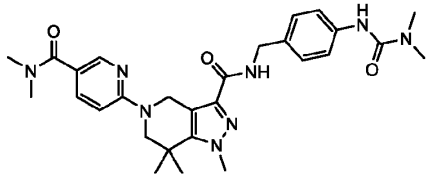
93	Ex. 1[a]		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-hydroxy-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3
94	Ex. 43		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(oxetan-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.63 (t, 1H), 8.26 – 8.19 (m, 2H), 7.63 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.22 – 7.16 (m, 2H), 6.89 (d, 1H), 5.61 – 5.46 (m, 1H), 4.97 (t, 2H), 4.87 (t, 2H), 4.76 (s, 2H), 4.41 – 4.30 (m, 2H), 3.92 (t, 2H), 2.96 (s, 6H), 2.90 (s, 6H), 2.80 – 2.72 (m, 2H).

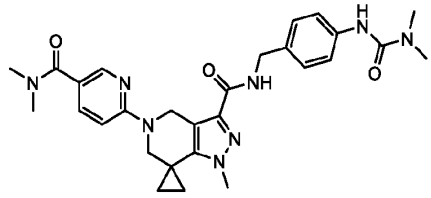
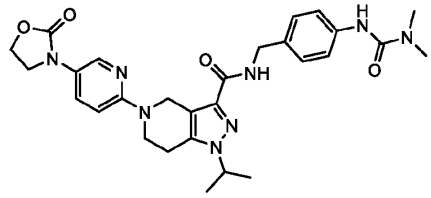
95	Ex. 43		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, 1H), 7.63 (dd, 1H), 7.38 – 7.33 (m, 2H), 7.32 – 7.28 (m, 2H), 7.14 (t, 1H), 6.78 (d, 1H), 6.31 (s, 1H), 4.98 (d, 1H), 4.85 – 4.78 (m, 1H), 4.58 – 4.53 (m, 2H), 4.46 – 4.36 (m, 2H), 3.34 (dd, 1H), 3.09 (s, 7H), 3.03 (s, 6H), 1.48 – 1.44 (m, 6H), 1.30 – 1.26 (m, 3H).
96	Ex. 43		1-cyclobutyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	545.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.27 – 8.19 (m, 2H), 7.63 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 6.88 (d, 1H), 4.85 – 4.69 (m, 3H), 4.35 (d, 2H), 3.92 (t, 2H), 2.96 (s, 6H), 2.90 (s, 6H), 2.77 (t, 2H), 2.61 – 2.52 (m, 2H), 2.37 – 2.28 (m, 2H), 1.83 – 1.71 (m, 2H).

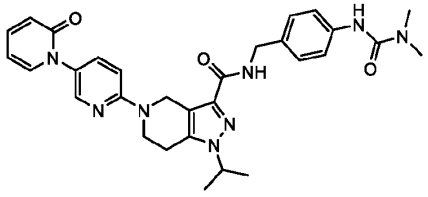
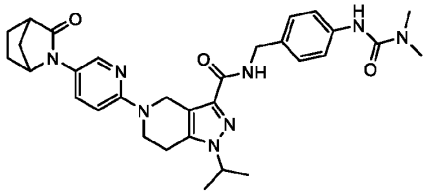
97	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-5-azaspiro[2.4]heptan-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	571.4
98	Ex. 1[a]		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-fluoro-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	563.4

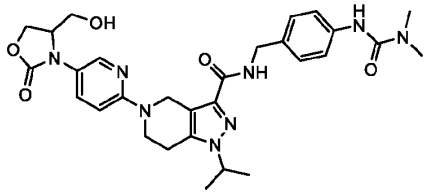
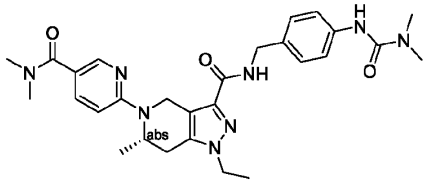
99	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methyl-2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.4
100	Ex. 1[ac]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-oxo-1,4-oxazepan-4-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4

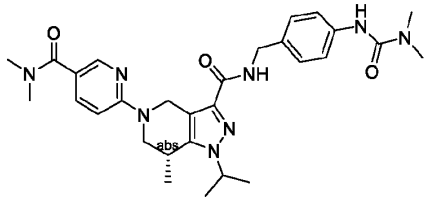
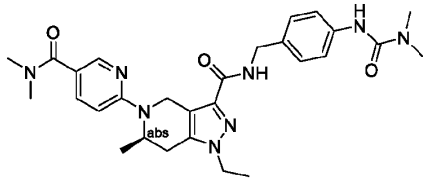
101	Ex. 43		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.48 (t, 1H), 8.27 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 6.91 (d, 1H), 5.45 – 5.31 (m, 1H), 4.92 – 4.61 (m, 2H), 4.35 (d, 2H), 4.14 – 4.04 (m, 1H), 3.88 – 3.77 (m, 1H), 2.99 – 2.93 (m, 7H), 2.91 (s, 6H), 2.77 – 2.64 (m, 1H), 1.71 (d, 3H).
102	Ex. 102		*N*-(4-aminobenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	462.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.24 (d, 1H), 8.13 (t, 1H), 7.64 (dd, 1H), 7.03 – 6.96 (m, 2H), 6.88 (d, 1H), 6.52 – 6.46 (m, 2H), 4.95 (s, 2H), 4.78 – 4.69 (m, 2H), 4.54 – 4.41 (m, 1H), 4.24 (d, 2H), 3.94 (t, 2H), 2.97 (s, 6H), 2.81 (t, 2H), 1.38 (d, 6H).
103	Ex. 1[ac]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxomorpholino)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3

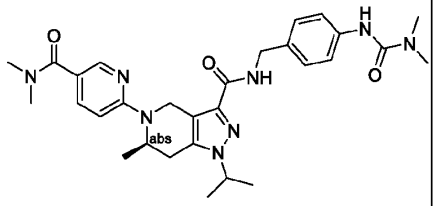
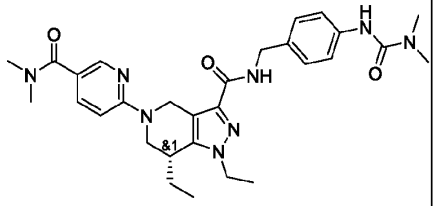
104	Ex. 9		1-(bicyclo[1.1.1]pentan-1-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	557.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, 1H), 7.61 (dd, 1H), 7.38 – 7.31 (m, 2H), 7.29 – 7.24 (m, 2H), 6.75 (d, 1H), 4.75 (s, 2H), 4.53 (s, 2H), 4.13 – 4.08 (m, 2H), 3.07 (s, 6H), 3.02 (s, 6H), 2.90 – 2.85 (m, 2H), 2.59 (s, 1H), 2.31 (s, 6H).
105	Ex. 43		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7,7-trimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, 1H), 7.62 (dd, 1H), 7.37 – 7.32 (m, 2H), 7.29 – 7.26 (m, 2H), 7.08 (t, 1H), 6.77 (d, 1H), 6.33 (s, 1H), 4.70 (s, 2H), 4.54 (d, 2H), 3.90 (s, 3H), 3.84 (s, 2H), 3.08 (s, 6H), 3.03 (s, 6H), 1.37 (s, 6H).

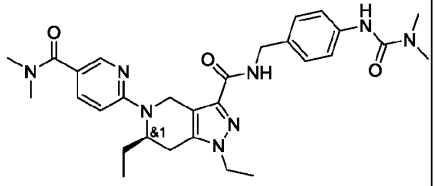
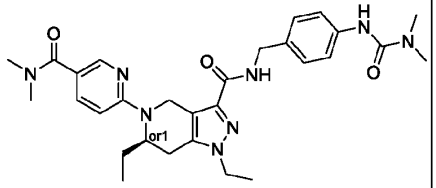
106	Ex. 5		5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-methyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide	531.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.24 – 8.19 (m, 2H), 7.61 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.19 – 7.12 (m, 2H), 6.88 (d, 1H), 4.81 (s, 2H), 4.32 (d, 2H), 3.74 (s, 2H), 3.67 (s, 3H), 2.97 (s, 6H), 2.90 (s, 6H), 1.42 (t, 2H), 1.02 (t, 2H).
107	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.4

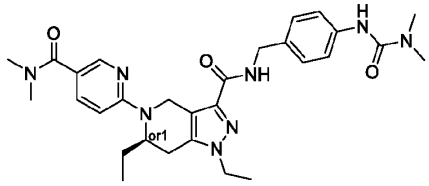
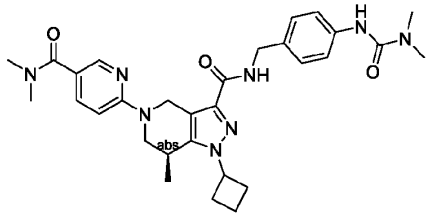
108	Ex. 145		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	555.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.24 (s, 1H), 8.11 (d, 1H), 7.66 – 7.60 (m, 2H), 7.53 – 7.46 (m, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 7.01 (d, 1H), 6.48 – 6.44 (m, 1H), 6.33 – 6.27 (m, 1H), 4.75 (s, 2H), 4.55 – 4.44 (m, 1H), 4.34 (d, 2H), 3.95 (t, 2H), 2.90 (s, 6H), 2.87 – 2.81 (m, 2H), 1.39 (d, 6H).
109	Ex. 1[ac]		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxo-2-azabicyclo[2.2.1]heptan-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	571.4

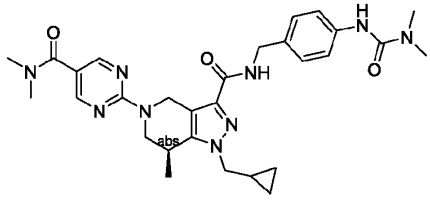
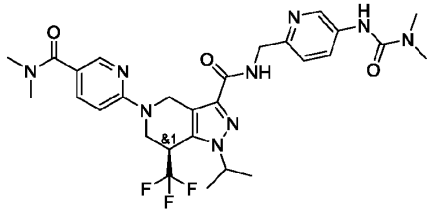
110	Ex. 1[a]		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-(hydroxymethyl)-2-oxooxazolidin-3-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	577.4
111 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.26 (d, 1H), 8.22 (s, 1H), 7.65 (dd, 1H), 7.40 – 7.35 (m, 2H), 7.20 – 7.14 (m, 2H), 6.84 (d, 1H), 5.31 – 5.22 (m, 1H), 5.14 (d, 1H), 4.32 (d, 2H), 4.17 – 4.02 (m, 3H), 3.01 – 2.92 (m, 7H), 2.90 (s, 6H), 2.73 (d, 1H), 1.32 (t, 3H), 1.06 (d, 3H).

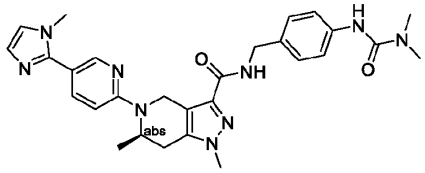
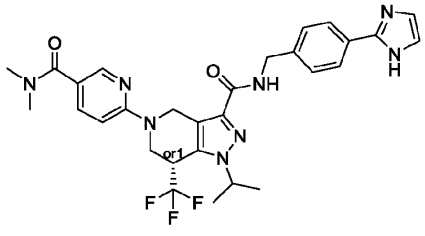
112 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, 1H), 7.63 (dd, 1H), 7.38 – 7.33 (m, 2H), 7.32 – 7.28 (m, 2H), 7.17 – 7.12 (m, 1H), 6.81 – 6.76 (m, 1H), 6.34 – 6.28 (m, 1H), 5.01 – 4.93 (m, 1H), 4.85 – 4.76 (m, 1H), 4.57 – 4.53 (m, 2H), 4.46 – 4.34 (m, 2H), 3.37 – 3.30 (m, 1H), 3.09 (s, 7H), 3.03 (s, 6H), 1.51 – 1.41 (m, 6H), 1.30 – 1.25 (m, 3H).
113	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.26 (d, 1H), 8.23 (s, 1H), 7.65 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.21 – 7.15 (m, 2H), 6.85 (d, 1H), 5.31 – 5.22 (m, 1H), 5.14 (d, 1H), 4.33 (d, 2H), 4.17 – 4.01 (m, 3H), 3.01 – 2.93 (m, 7H), 2.90 (s, 6H), 2.77 – 2.69 (m, 1H), 1.32 (t, 3H), 1.06 (d, 3H).

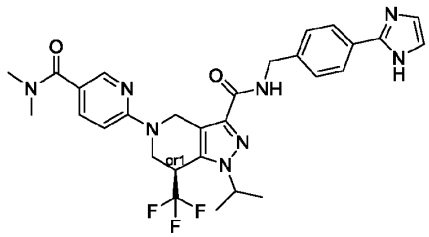
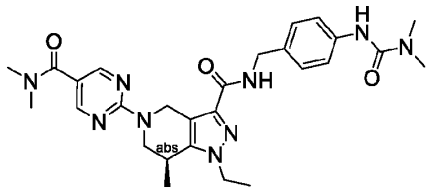
114	Ex. 113[d]		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.36 (t, 1H), 8.27 – 8.25 (m, 1H), 8.23 (s, 1H), 7.67 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.21 – 7.16 (m, 2H), 6.87 (d, 1H), 5.29 – 5.21 (m, 1H), 5.13 (d, 1H), 4.56 – 4.47 (m, 1H), 4.38 – 4.30 (m, 2H), 4.18 – 4.09 (m, 1H), 3.00 – 2.95 (m, 7H), 2.92 – 2.89 (m, 6H), 2.77 (d, 1H), 1.41 (dd, 6H), 1.07 (d, 3H).
115	Ex. 113[d]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.26 – 8.20 (m, 2H), 7.66 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.15 (m, 2H), 6.85 (d, 1H), 5.00 (d, 1H), 4.76 (d, 1H), 4.39 – 4.28 (m, 2H), 4.24 (d, 1H), 4.15 – 4.05 (m, 2H), 3.21 – 3.16 (m, 1H), 3.04 – 2.94 (m, 7H), 2.90 (s, 6H), 1.62 – 1.53 (m, 1H), 1.48 – 1.37 (m, 4H), 1.03 (t, 3H).

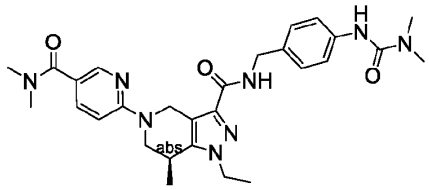
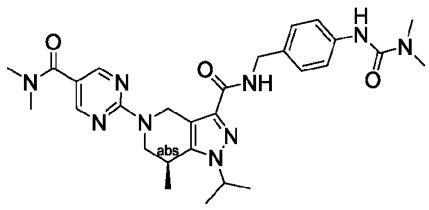
116	Ex. 128[de]		*rac-(R)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.25 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.20 – 7.14 (m, 2H), 6.88 (d, 1H), 5.23 (d, 1H), 5.02 (s, 1H), 4.38 – 4.28 (m, 2H), 4.17 – 4.03 (m, 3H), 3.02 – 2.94 (m, 6H), 2.93 – 2.86 (m, 7H), 2.80 (d, 1H), 1.55 – 1.40 (m, 2H), 1.32 (t, 3H), 0.80 (t, 3H).
117 ^	Ex. 128[de]		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.25 – 8.21 (m, 2H), 7.63 (dd, 1H), 7.40 – 7.36 (m, 2H), 7.19 – 7.15 (m, 2H), 6.86 (d, 1H), 5.23 (d, 1H), 5.02 (s, 1H), 4.37 – 4.28 (m, 2H), 4.16 – 4.02 (m, 3H), 2.97 (s, 6H), 2.93 – 2.87 (m, 7H), 2.83 – 2.77 (m, 1H), 1.55 – 1.38 (m, 2H), 1.31 (t, 3H), 0.80 (t, 3H).

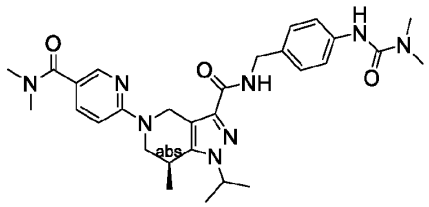
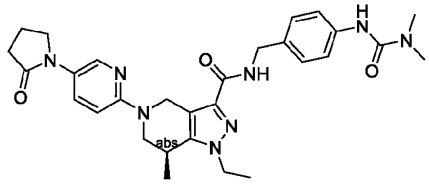
118 ^	Ex. 128[de]		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.25 – 8.21 (m, 2H), 7.63 (dd, 1H), 7.40 – 7.36 (m, 2H), 7.19 – 7.15 (m, 2H), 6.86 (d, 1H), 5.23 (d, 1H), 5.03 (s, 1H), 4.38 – 4.27 (m, 2H), 4.16 – 4.02 (m, 3H), 2.97 (s, 6H), 2.93 – 2.86 (m, 7H), 2.82 – 2.77 (m, 1H), 1.56 – 1.39 (m, 2H), 1.31 (t, 3H), 0.80 (t, 3H).
119 ^	Ex. 113		(*S*)-1-cyclobutyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.50 – 8.43 (m, 1H), 8.21 (s, 2H), 7.61 (d, 1H), 7.40 – 7.33 (m, 2H), 7.16 (d, 2H), 6.86 (d, 1H), 5.04 (d, 1H), 4.90 – 4.77 (m, 1H), 4.41 – 4.18 (m, 4H), 3.23 – 3.11 (m, 2H), 2.95 (s, 6H), 2.88 (s, 6H), 2.78 – 2.62 (m, 2H), 2.39 – 2.26 (m, 2H), 1.85 – 1.69 (m, 2H), 1.14 (d, 3H).

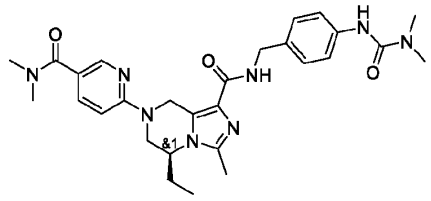
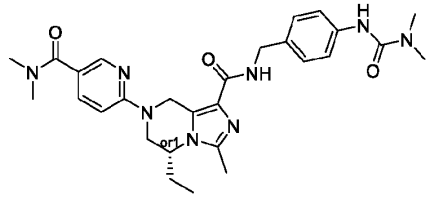
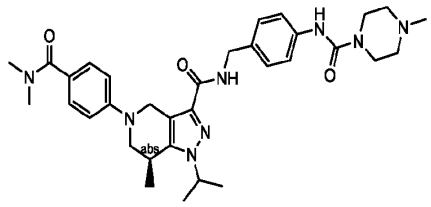
120	Ex. 77		(*S*)-1-(cyclopropylmethyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	560.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.55 – 8.48 (m, 2H), 8.42 (t, 1H), 8.23 (s, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 5.44 (d, 1H), 4.76 – 4.67 (m, 1H), 4.42 – 4.27 (m, 3H), 4.11 – 4.01 (m, 1H), 3.93 – 3.80 (m, 1H), 3.49 – 3.41 (m, 1H), 3.29 – 3.20 (m, 1H), 3.00 (s, 6H), 2.92 – 2.87 (m, 6H), 1.35 – 1.22 (m, 1H), 1.16 (d, 3H), 0.58 – 0.46 (m, 2H), 0.45 – 0.37 (m, 2H).
121	**P44;** Ex. 30[f]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.6; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.65 – 8.61 (m, 2H), 8.53 (s, 1H), 8.28 – 8.26 (m, 1H), 7.92 – 7.85 (m, 1H), 7.68 (dd, 1H), 7.29 (d, 1H), 6.83 (d, 1H), 5.28 (d, 1H), 5.06 (d, 1H), 4.74 – 4.65 (m, 1H), 4.58 – 4.45 (m, 3H), 4.30 – 4.23 (m, 1H), 3.30 – 3.28 (m, 1H), 2.98 (s, 6H), 2.93 (s, 6H), 1.45 (dd, 6H).

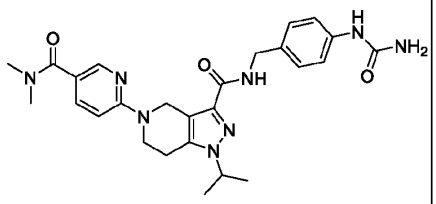
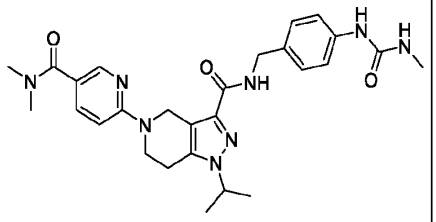
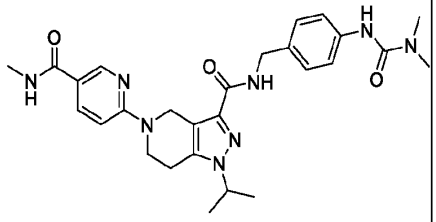
122 ^	Ex. 42		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.50 (t, 1H), 8.46 (d, 1H), 8.22 (s, 1H), 7.87 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.21 – 7.14 (m, 3H), 6.96 – 6.91 (m, 2H), 5.32 – 5.22 (m, 1H), 5.21 – 5.13 (m, 1H), 4.41 – 4.26 (m, 2H), 4.10 (d, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 3.01 – 2.88 (m, 7H), 2.77 – 2.65 (m, 1H), 1.09 (d, 3H).
123 ^	Ex. 30[f]		*rel*-(*R* or *S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	581.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 12.45 (s, 1H), 8.72 – 8.67 (m, 1H), 8.31 – 8.26 (m, 1H), 7.90 – 7.85 (m, 2H), 7.72 – 7.67 (m, 1H), 7.41 – 7.36 (m, 2H), 7.27 – 6.96 (m, 2H), 6.88 – 6.81 (m, 1H), 5.28 (d, 1H), 5.07 (d, 1H), 4.73 – 4.64 (m, 1H), 4.59 – 4.40 (m, 3H), 4.33 – 4.24 (m, 1H), 3.29 – 3.27 (m, 1H), 2.98 (s, 6H), 1.50 – 1.40 (m, 6H).

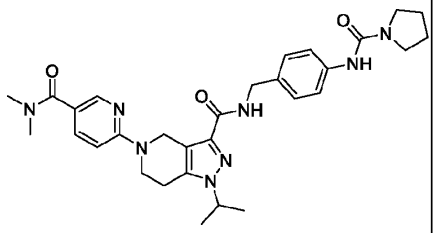
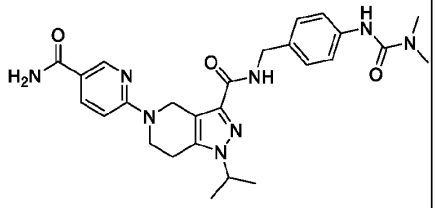
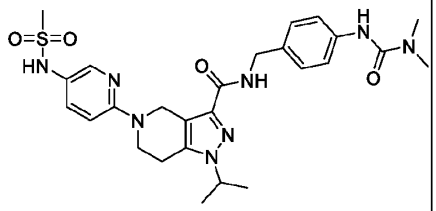
124 ^	Ex. 30[f]		*rel*-(*R* or *S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	581.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 12.45 (s, 1H), 8.69 (t, 1H), 8.27 (d, 1H), 7.90 – 7.85 (m, 2H), 7.69 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.27 – 6.96 (m, 2H), 6.84 (d, 1H), 5.28 (d, 1H), 5.07 (d, 1H), 4.72 – 4.64 (m, 1H), 4.58 – 4.40 (m, 3H), 4.29 (d, 1H), 3.31 – 3.28 (m, 1H), 2.98 (s, 6H), 1.50 – 1.38 (m, 6H).
125	Ex. 125		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	534.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (s, 2H), 8.45 (t, 1H), 8.23 (s, 1H), 7.41 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 5.41 (d, 1H), 4.67 (dd, 1H), 4.42 – 4.26 (m, 3H), 4.16 – 4.04 (m, 2H), 3.48 (dd, 1H), 3.28 – 3.19 (m, 1H), 2.99 (br s, 6H), 2.90 (s, 6H), 1.38 (t, 3H), 1.16 (d, 3H).

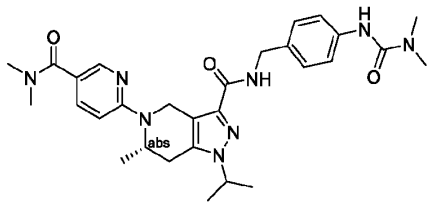
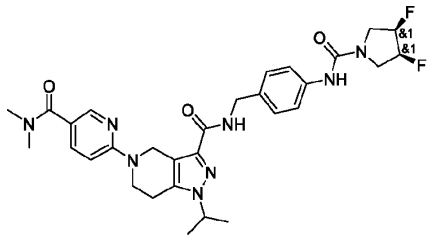
126	Ex. 126		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.25 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 6.89 (d, 1H), 5.05 (d, 1H), 4.41 – 4.25 (m, 4H), 4.17 – 4.04 (m, 2H), 3.43 – 3.36 (m, 1H), 3.26 – 3.17 (m, 1H), 2.98 (br s, 6H), 2.90 (s, 6H), 1.38 (t, 3H), 1.20 (d, 3H).
127 ^	Ex. 127		(*S*)-5-(5-dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.9; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (s, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 5.47 (d, 1H), 4.75 (dd, 1H), 4.58 – 4.46 (m, 1H), 4.40 – 4.29 (m, 3H), 3.42 (dd, 1H), 3.29 – 3.23 (m, 1H) 3.04 - 2.94 (m, 6H), 2.91 (s, 6H), 1.38 (dd, 6H), 1.11 (d, 3H).

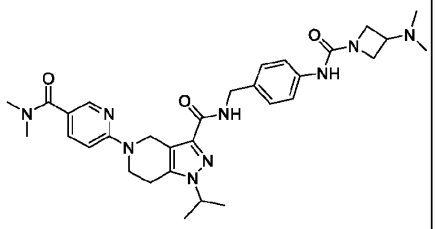
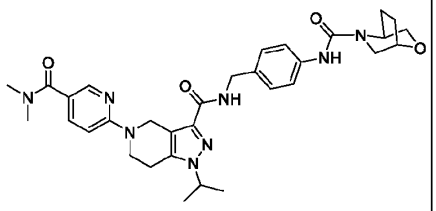
128 ^	Ex. 128		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.18 – 8.16 (m, 2H), 7.57 (dd, 1H), 7.34 – 7.29 (m, 2H), 7.14 – 7.08 (m, 2H), 6.82 (d, 1H), 5.03 (d, 1H), 4.50 – 4.41 (m, 1H), 4.39 – 4.23 (m, 3H), 4.17 (d, 1H), 3.36 – 3.35 (m, 1H), 3.18 – 3.12 (m, 1H), 2.91 (s, 6H), 2.84 (s, 6H), 1.35 (dd, 6H), 1.13 (d, 3H).
129	Ex. 77		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	545.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.40 (t, 1H), 8.25 (d, 1H), 8.19 (s, 1H), 7.84 (dd, 1H), 7.37 – 7.31 (m, 2H), 7.16 – 7.10 (m, 2H), 6.86 (d, 1H), 4.86 (d, 1H), 4.32 – 4.26 (m, 2H), 4.24 – 4.14 (m, 2H), 4.10 – 4.00 (m, 2H), 3.77 – 3.70 (m, 2H), 3.18 – 3.11 (m, 1H), 2.87 (s, 6H), 2.42 – 2.37 (m, 3H), 2.07 – 1.96 (m, 2H), 1.35 (t, 3H), 1.18 (d, 3H).

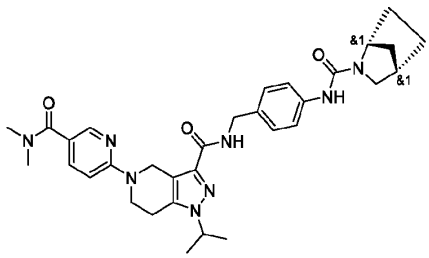
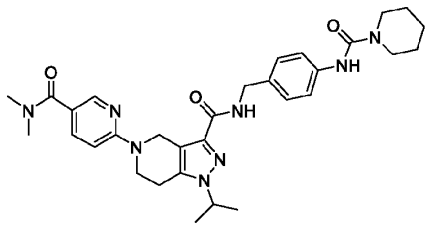
130	Ex. 23[g]		*rac*-(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5-ethyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	533.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.34 (d, 1H), 7.76 (dd, 1H), 7.38 – 7.33 (m, 2H), 7.30 – 7.25 (m, 2H), 6.91 (d, 1H), 5.32 – 5.12 (m, 2H), 4.71 – 4.63 (m, 1H), 4.61 – 4.55 (m, 1H), 4.51 (s, 2H), 4.37 – 4.28 (m, 1H), 3.15 – 3.08 (m, 6H), 3.02 (s, 6H), 2.42 (s, 3H), 1.80 – 1.69 (m, 2H), 1.09 (t, 3H).
131 ^	Ex. 23[g]		*rel-(R* or *S*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5-ethyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	533.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.35 – 8.30 (m, 1H), 7.77 – 7.70 (m, 1H), 7.36 – 7.30 (m, 2H), 7.28 – 7.22 (m, 2H), 6.88 (d, 1H), 5.29 – 5.10 (m, 2H), 4.72 – 4.55 (m, 2H), 4.54 – 4.45 (m, 2H), 4.35 – 4.26 (m, 1H), 3.09 (s, 6H), 3.00 (s, 6H), 2.40 (s, 3H), 1.79 – 1.66 (m, 2H), 1.06 (t, 3H).
132	Ex. 132		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (s, 1H), 8.36 (t, 1H), 7.40 – 7.28 (m, 4H), 7.21 – 7.12 (m, 2H), 7.00 – 6.91 (m, 2H), 4.59 – 4.48 (m, 2H), 4.36 – 4.30 (m, 2H), 4.10 (d, 1H), 3.85 – 3.77 (m, 1H), 3.41 (t, 4H), 3.28 – 3.16 (m, 2H), 2.97 – 2.91 (m, 6H), 2.29 (t, 4H), 2.18 (s, 3H), 1.47 – 1.37 (m, 6H), 1.28 (d, 3H).

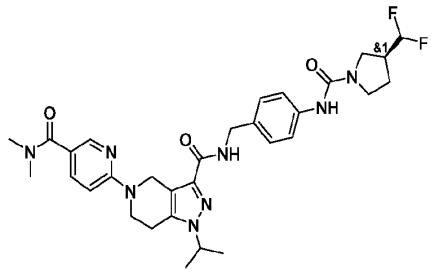
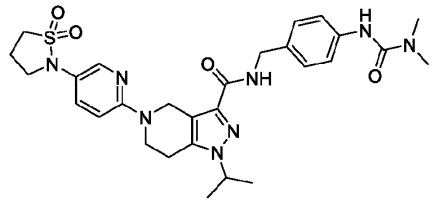
133	Ex. 113		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	505.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.42 (s, 1H), 8.27 (t, 1H), 8.18 (d, 1H), 7.58 (dd, 1H), 7.29 – 7.24 (m, 2H), 7.15 – 7.09 (m, 2H), 6.83 (d, 1H), 5.73 (s, 2H), 4.69 (s, 2H), 4.49 – 4.38 (m, 1H), 4.28 (d, 2H), 3.89 (t, 2H), 2.91 (s, 6H), 2.76 (t, 2H), 1.34 (d, 6H).
134	Ex. 113		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.40 (s, 1H), 8.27 (t, 1H), 8.19 (d, 1H), 7.59 (dd, 1H), 7.30 – 7.24 (m, 2H), 7.15 – 7.10 (m, 2H), 6.84 (d, 1H), 5.91 (q, 1H), 4.70 (s, 2H), 4.50 – 4.36 (m, 1H), 4.28 (d, 2H), 3.90 (t, 2H), 2.92 (s, 6H), 2.77 (t, 2H), 2.57 (d, 3H), 1.34 (d, 6H).
135	Ex. 43		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(methylcarbamoyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (d, 1H), 8.29 (t, 1H), 8.21 – 8.13 (m, 2H), 7.88 (dd, 1H), 7.35 – 7.30 (m, 2H), 7.14 – 7.07 (m, 2H), 6.83 (d, 1H), 4.69 (s, 2H), 4.48 – 4.36 (m, 1H), 4.28 (d, 2H), 3.90 (t, 2H), 2.84 (s, 6H), 2.75 (t, 2H), 2.68 (d, 3H), 1.32 (d, 6H).

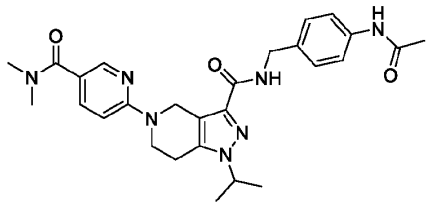
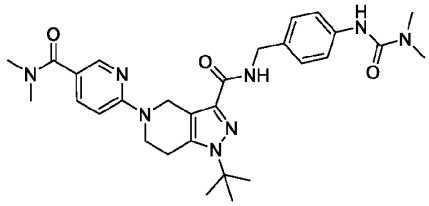
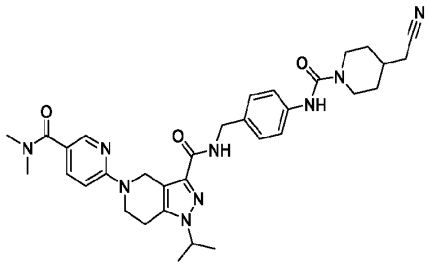
136	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.4
137	Ex. 193		5-(5-carbamoylpyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	505.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (d, 1H), 8.34 (t, 1H), 8.23 (s, 1H), 7.97 (dd, 1H), 7.80 – 7.71 (m, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.10 (m, 3H), 6.88 (d, 1H), 4.76 (s, 2H), 4.55 – 4.42 (m, 1H), 4.34 (d, 2H), 3.96 (t, 2H), 2.90 (s, 6H), 2.83 – 2.77 (m, 2H), 1.38 (d, 6H).
138	Ex. 1		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(methylsulfonamido)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	555.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.03 (d, 1H), 7.51 (dd, 1H), 7.35 – 7.30 (m, 2H), 7.28 – 7.22 (m, 2H), 6.87 (d, 1H), 4.66 (s, 2H), 4.54 – 4.44 (m, 3H), 3.96 (t, 2H), 2.99 (s, 6H), 2.88 (s, 3H), 2.83 (t, 2H), 1.44 (d, 6H).

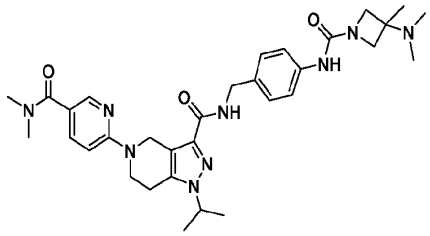
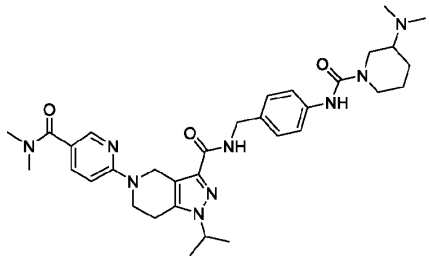
139	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.28 (d, 1H), 8.24 (s, 1H), 7.67 (dd, 1H), 7.44 – 7.38 (m, 2H), 7.23 – 7.19 (m, 2H), 6.86 (d, 1H), 5.33 – 5.23 (m, 1H), 5.15 (d, 1H), 4.59 – 4.49 (m, 1H), 4.36 (d, 2H), 4.12 (d, 1H), 3.03 – 2.95 (m, 7H), 2.92 (s, 6H), 2.81 – 2.74 (m, 1H), 1.42 (dd, 6H), 1.08 (d, 3H).
140	Ex. 136		*N*-(4-((3*R*,4*S*)-3,4-difluoropyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	595.5

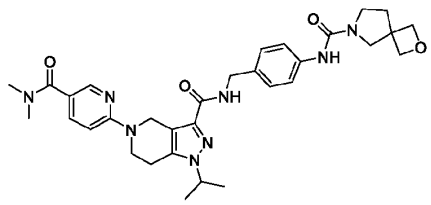
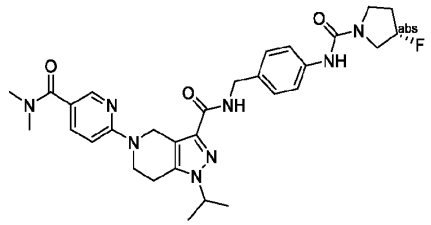
141	Ex. 136		*N*-(4-(3-(dimethylamino)azetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	588.5
142	Ex. 136		(1*S*,4*S*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-oxa-5-azabicyclo[2.2.2]octane-5-carboxamide	601.5

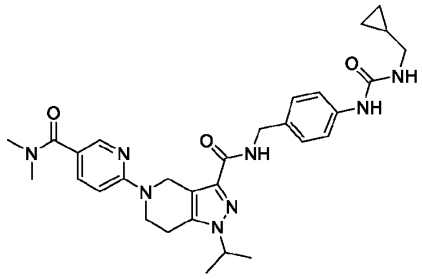
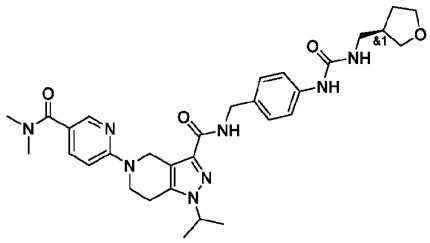
143	Ex. 136		*rac-N*-(4-((1*R*,4*S*)-2-azabicyclo[2.2.1]heptane-2-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	585.6
144	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.5

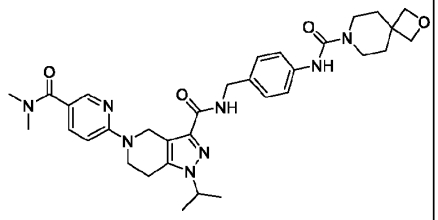
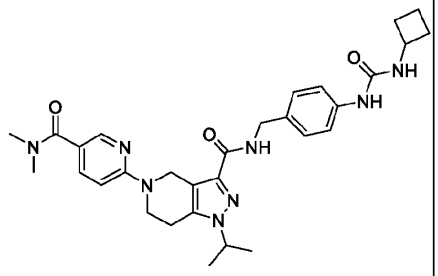
145	Ex. 136		*rac*-(*R*)-*N*-(4-(3-(difluoromethyl)pyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	609.5
146	Ex. 1		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(1,1-dioxidoisothiazolidin-2-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	581.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.20 (s, 1H), 7.99 (d, 1H), 7.50 (dd, 1H), 7.38 – 7.31 (m, 2H), 7.17 – 7.11 (m, 2H), 6.90 (d, 1H), 4.63 (s, 2H), 4.50 – 4.40 (m, 1H), 4.30 (d, 2H), 3.84 (t, 2H), 3.60 (t, 2H), 3.41 – 3.35 (m, 2H), 2.87 (s, 6H), 2.77 (t, 2H), 2.38 – 2.27 (m, 2H), 1.35 (d, 6H).

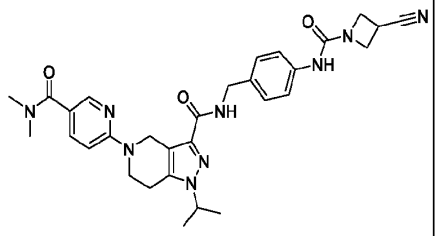
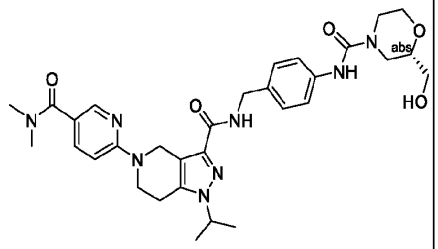
147	Ex. 113		*N*-(4-acetamidobenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	504.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.87 (s, 1H), 8.36 (t, 1H), 8.20 (d, 1H), 7.60 (dd, 1H), 7.50 – 7.42 (m, 2H), 7.20 (d, 2H), 6.85 (d, 1H), 4.71 (s, 2H), 4.51 – 4.37 (m, 1H), 4.32 (d, 2H), 3.91 (t, 2H), 2.93 (s, 6H), 2.77 (t, 2H), 1.98 (s, 3H), 1.36 (d, 6H).
148	Ex. 113		1-(*tert*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.27 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.17 (d, 2H), 6.87 (d, 1H), 4.74 (s, 2H), 4.35 (d, 2H), 3.94 – 3.88 (m, 2H), 3.04 – 2.99 (m, 2H), 2.97 (s, 6H), 2.90 (s, 6H), 1.57 (s, 9H).
149	Ex. 136		*N*-(4-(4-(cyanomethyl)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.6

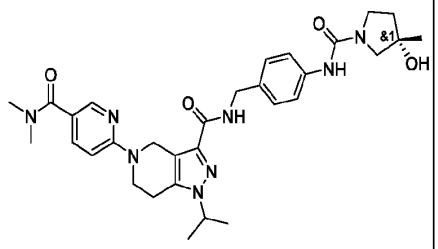
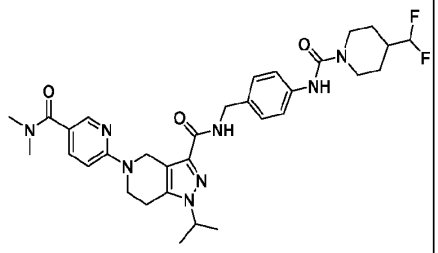
150	Ex. 136		*N*-(4-(3-(dimethylamino)-3-methylazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.5
151	Ex. 136		*N*-(4-(3-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.6

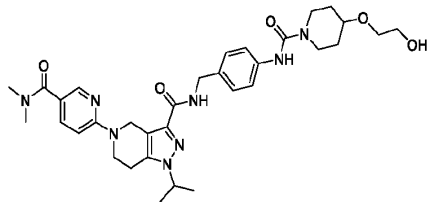
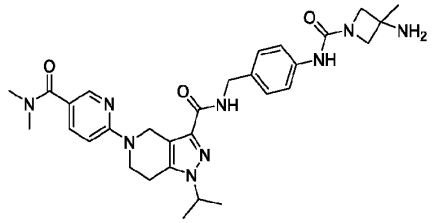
152	Ex. 136		*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-oxa-6-azaspiro[3.4]octane-6-carboxamide	601.5
153	Ex. 136		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-fluoropyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	577.5

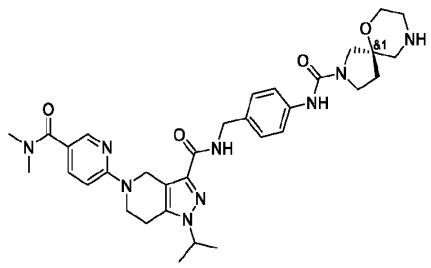
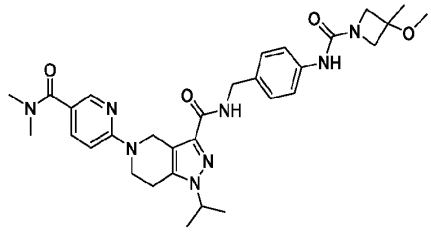
154	Ex. 136		*N*-(4-(3-(cyclopropylmethyl)ureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.5
155	Ex. 136		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-((tetrahydrofuran-3-yl)methyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.5

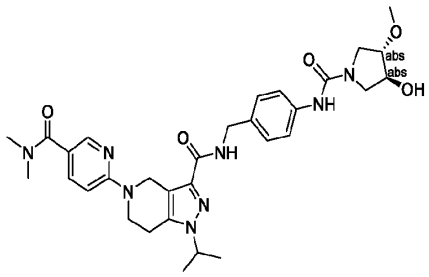
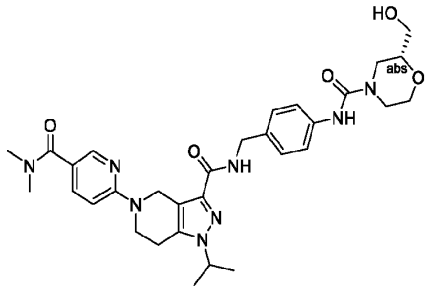
156	Ex. 136		*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-oxa-7-azaspiro[3.5]nonane-7-carboxamide	615.5
157	Ex. 136		*N*-(4-(3-cyclobutylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.5

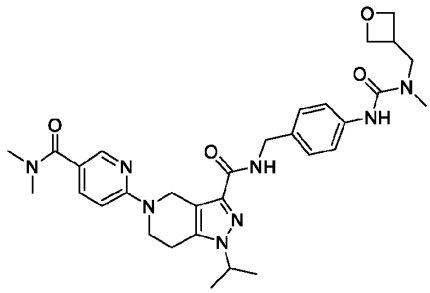
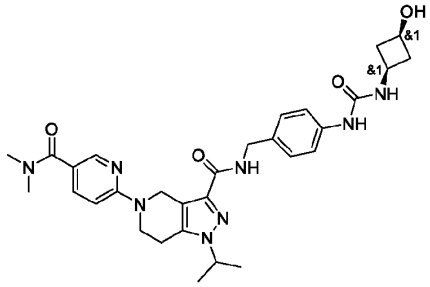
158	Ex. 136		*N*-(4-(3-cyanoazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	570.5
159	Ex. 136		(*S*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-(hydroxymethyl)morpholine-4-carboxamide	605.5

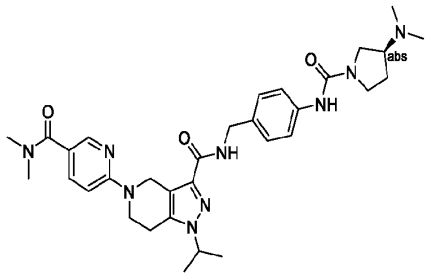
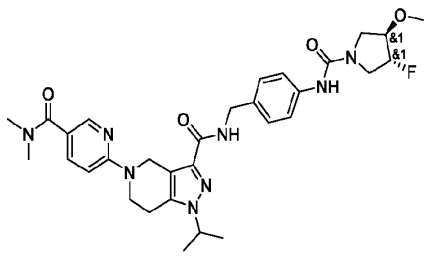
160	Ex. 136		*rac-(R)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-hydroxy-3-methylpyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.5
161	Ex. 136		*N*-(4-(4-(difluoromethyl)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	623.5

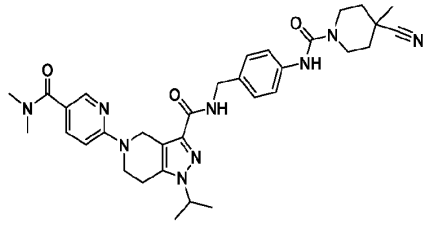
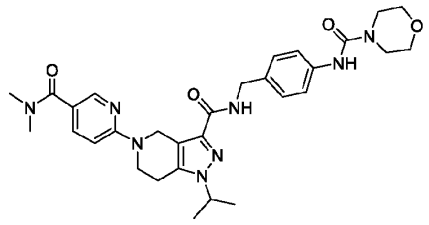
162	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(4-(2-hydroxyethoxy)piperidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.5
163	Ex. 136		*N*-(4-(3-amino-3-methylazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	574.5

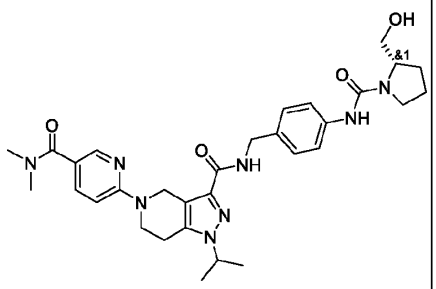
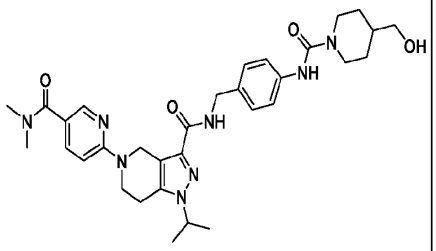
164	Ex. 136		*rac*-(*R*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-6-oxa-2,9-diazaspiro[4.5]decane-2-carboxamide	630.6
165	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methoxy-3-methylazetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4

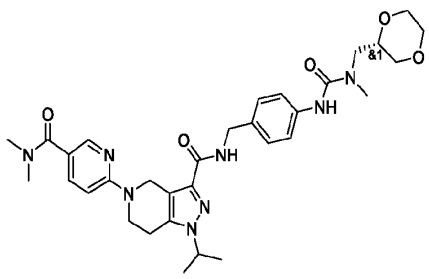
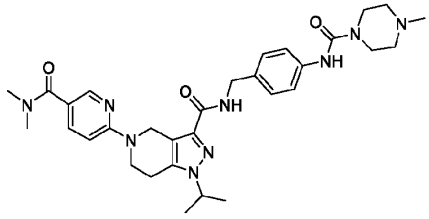
166	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-((3*S*,4*S*)-3-hydroxy-4-methoxypyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	605.4
167	Ex. 136		(*R*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-(hydroxymethyl)morpholine-4-carboxamide	605.4

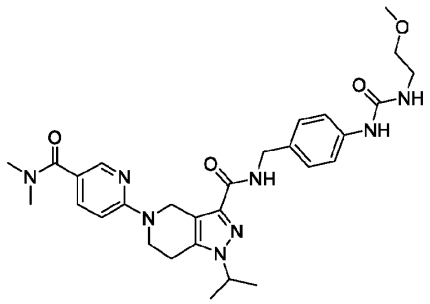
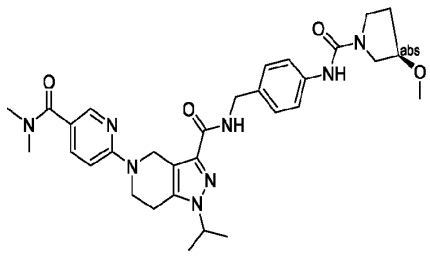
168	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methyl-3-(oxetan-3-ylmethyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4
169	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-((1*s*,3*s*)-3-hydroxycyclobutyl)ureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4

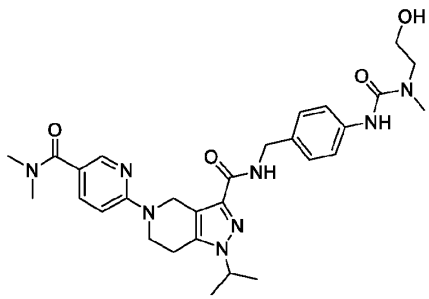
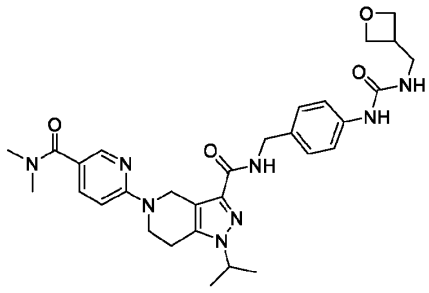
170	Ex. 136		(*S*)-*N*-(4-(3-(dimethylamino)pyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.5
171	Ex. 136		*rac*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-((3*R*,4*R*)-3-fluoro-4-methoxypyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	607.4

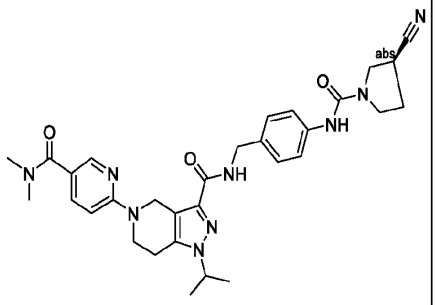
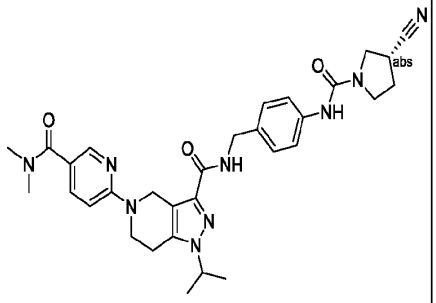
172	Ex. 136		*N*-(4-(4-cyano-4-methylpiperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.4
173	Ex. 136		*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)morpholine-4-carboxamide	575.4

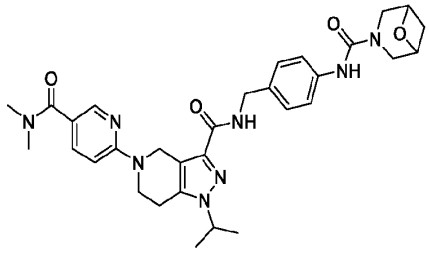
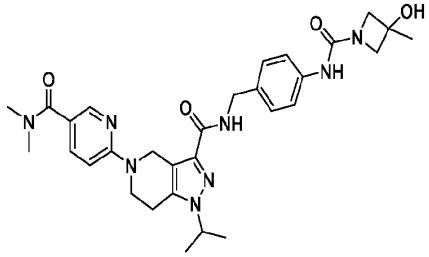
174	Ex. 136		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(2-(hydroxymethyl)pyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4
175	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(4-(hydroxymethyl)piperidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.4

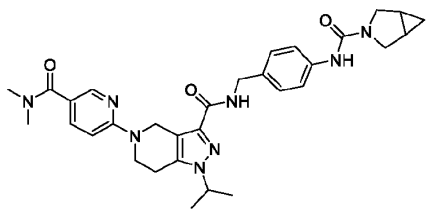
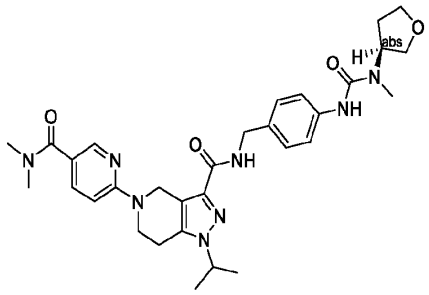
176	Ex. 136		*rac*-(*R*)-*N*-(4-(3-((1,4-dioxan-2-yl)methyl)-3-methylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	619.4
177	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	588.5

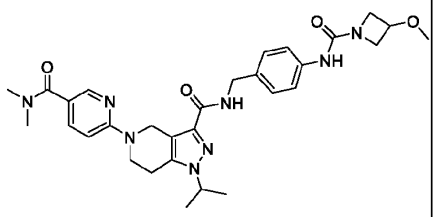
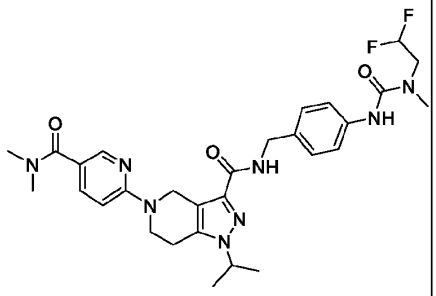
178	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-(2-methoxyethyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	563.4
179	Ex. 136		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methoxypyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4

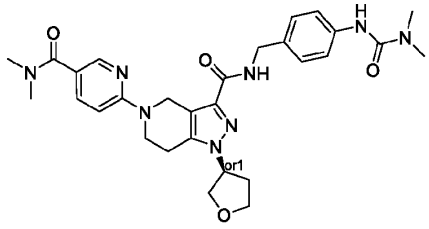
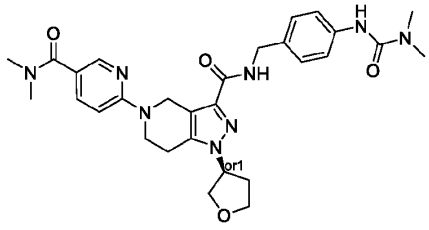
180	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-(2-hydroxyethyl)-3-methylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	563.4
181	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-(oxetan-3-ylmethyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4

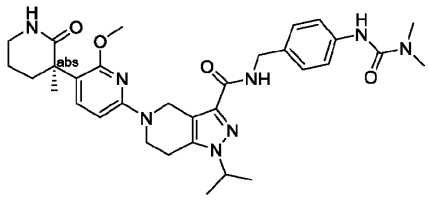
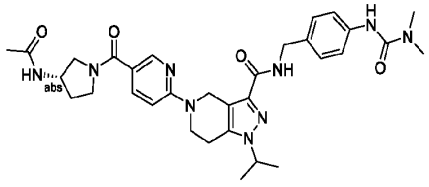
182	Ex. 136		(*S*)-*N*-(4-(3-cyanopyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	584.4
183	Ex. 136		(*R*)-*N*-(4-(3-cyanopyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	584.4

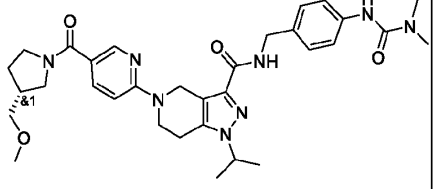
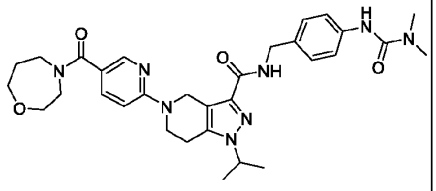
184	Ex. 136		*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-6-oxa-3-azabicyclo[3.1.1]heptane-3-carboxamide	587.4
185	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-hydroxy-3-methylazetidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4

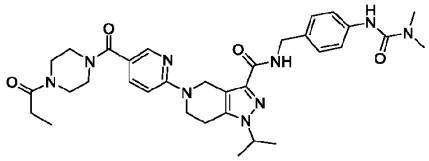
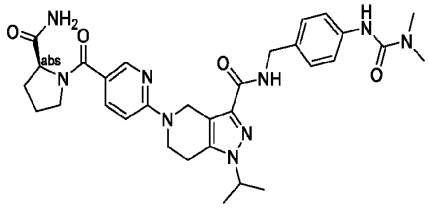
186	Ex. 136		*N*-(4-(3-azabicyclo[3.1.0]hexane-3-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	571.4
187	Ex. 136		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methyl-3-(tetrahydrofuran-3-yl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4

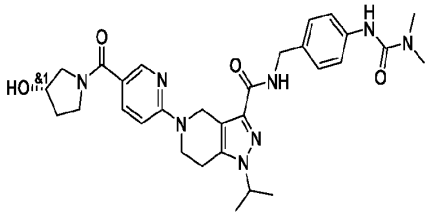
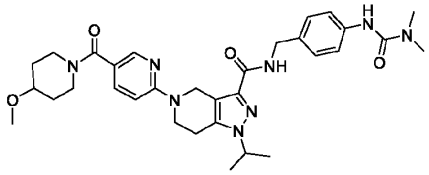
188	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methoxyazetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4
189	Ex. 136		*N*-(4-(3-(2,2-difluoroethyl)-3-methylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	583.4

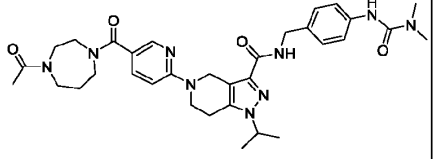
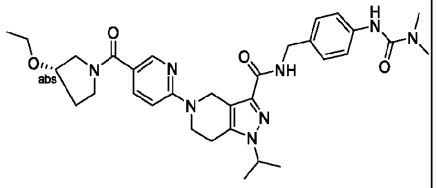
190 ^	Ex. 5		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydrofuran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.41 (t, 1H), 8.24 – 8.19 (m, 2H), 7.62 (dd, 1H), 7.40 – 7.34 (m, 2H), 7.17 – 7.12 (m, 2H), 6.88 (d, 1H), 5.04 – 4.90 (m, 1H), 4.74 (s, 2H), 4.32 (d, 2H), 4.09 – 3.74 (m, 6H), 2.95 (s, 6H), 2.89 (s, 6H), 2.84 – 2.78 (m, 2H), 2.33 – 2.24 (m, 2H).
191 ^	Ex. 5		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydrofuran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.44 – 8.39 (m, 1H), 8.24 – 8.21 (m, 2H), 7.63 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.16 (d, 2H), 6.89 (d, 1H), 5.06 – 4.93 (m, 1H), 4.75 (s, 2H), 4.34 (d, 2H), 4.13 – 3.75 (m, 6H), 2.96 (s, 6H), 2.90 (s, 6H), 2.85 – 2.80 (m, 2H), 2.34 – 2.25 (m, 2H).

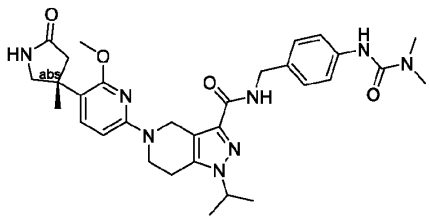
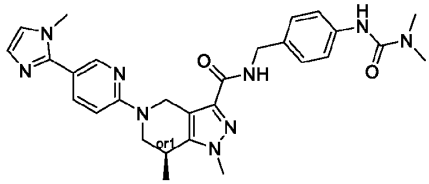
192	Ex. 12[h]		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(6-methoxy-5-(3-methyl-2-oxopiperidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.23 (s, 1H), 7.41 – 7.36 (m, 3H), 7.31 (d, 1H), 7.20 – 7.15 (m, 2H), 6.30 (d, 1H), 4.64 – 4.56 (m, 2H), 4.52 – 4.45 (m, 1H), 4.34 (d, 2H), 3.87 (t, 2H), 3.79 (s, 3H), 3.26 – 3.12 (m, 2H), 2.91 – 2.89 (m, 6H), 2.81 (t, 2H), 2.19 – 2.10 (m, 1H), 1.81 – 1.72 (m, 1H), 1.64 – 1.56 (m, 1H), 1.52 – 1.45 (m, 1H), 1.43 (s, 3H), 1.39 (d, 6H).
193	Ex. 193		(*S*)-5-(5-(3-acetamidopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.4

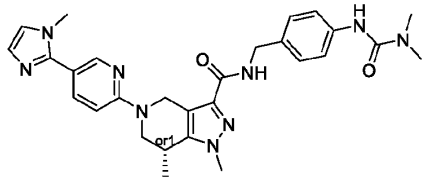
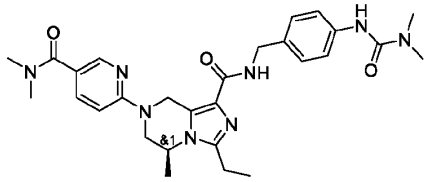
194	Ex. 193		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-(methoxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.9
195	Ex. 193		5-(5-(1,4-oxazepane-4-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.8

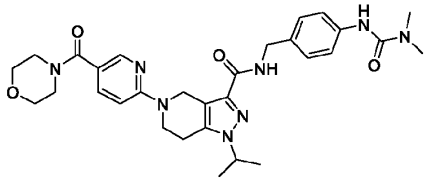
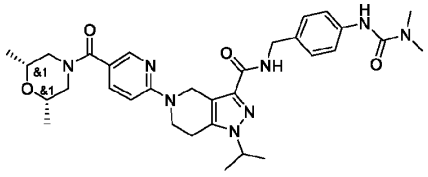
196	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-propionylpiperazine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	630.8
197	Ex. 193		(*S*)-5-(5-(2-carbamoylpyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.4

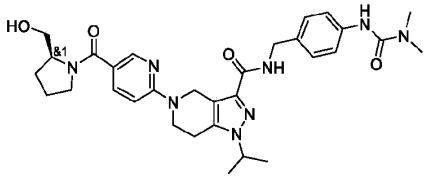
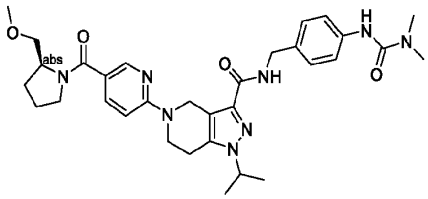
198	Ex. 193		*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxypyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4
199	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methoxypiperidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.4

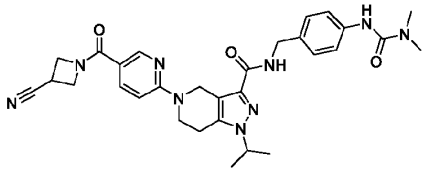
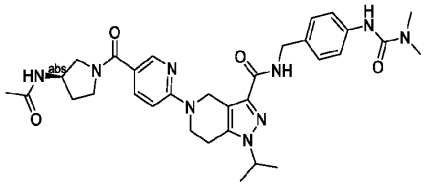
200	Ex. 193		5-(5-(4-acetyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	630.4
201	Ex. 193		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-ethoxypyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.4

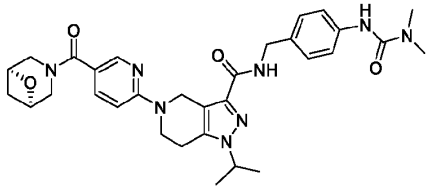
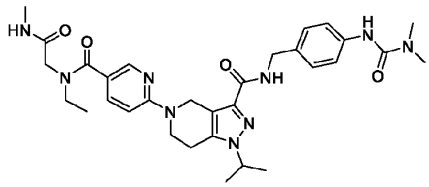
202	Ex. 132[r]		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(6-methoxy-5-(3-methyl-5-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.5
203 ^	Ex. 42		*rel-(R* or *S)-N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.38 (d, 1H), 8.18 (s, 1H), 7.80 (dd, 1H), 7.35 – 7.28 (m, 2H), 7.15 (d, 1H), 7.13 – 7.09 (m, 2H), 6.92 (d, 1H), 6.88 (d, 1H), 4.98 (d, 1H), 4.37 – 4.20 (m, 4H), 3.78 (s, 3H), 3.66 (s, 3H), 3.41 – 3.38 (m, 1H), 3.19 – 3.11 (m, 1H), 2.85 (s, 6H), 1.18 (d, 3H).

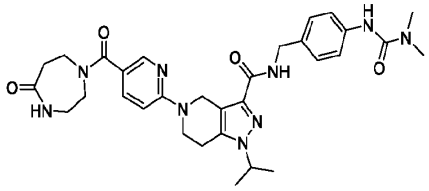
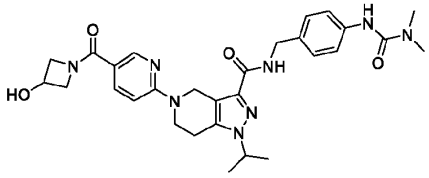
204 ^	Ex. 42		*rel-(R* or *S)-N-*(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.39 (d, 1H), 8.19 (s, 1H), 7.81 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.16 (d, 1H), 7.14 – 7.10 (m, 2H), 6.93 (d, 1H), 6.89 (d, 1H), 4.99 (d, 1H), 4.37 – 4.22 (m, 4H), 3.79 (s, 3H), 3.67 (s, 3H), 3.44 – 3.37 (m, 1H), 3.24 – 3.14 (m, 1H), 2.86 (s, 6H), 1.19 (d, 3H).
205	Ex. 5		*rac-*(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N-*(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	533.2; ^{1}H NMR* (400 MHz, CD_3OD) δ 8.31 (d, 1H), 7.74 (dd, 1H), 7.37 – 7.31 (m, 2H), 7.30 – 7.24 (m, 2H), 6.93 (d, 1H), 5.38 (d, 1H), 4.62 – 4.57 (m, 3H), 4.50 (s, 2H), 3.40 (dd, 1H), 3.10 (s, 6H), 3.02 – 2.98 (m, 6H), 2.83 – 2.67 (m, 2H), 1.41 – 1.33 (m, 6H).

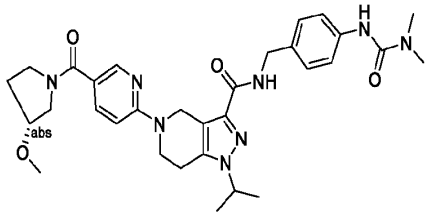
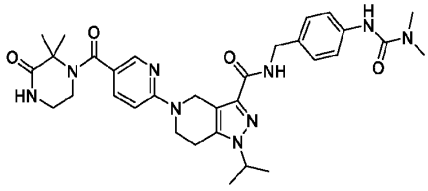
206	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(morpholine-4-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4
207	Ex. 193		5-(5-((2*R*,6*S*)-2,6-dimethylmorpholine-4-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.5

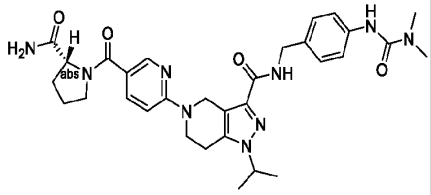
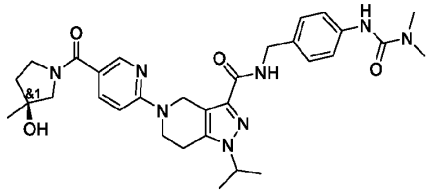
208	Ex. 193		*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-(hydroxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carbo*x*amide	589.5
209	Ex. 193		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methoxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.5

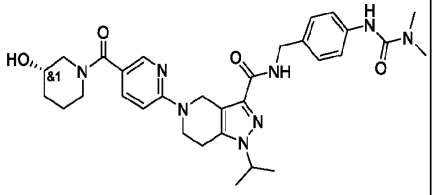
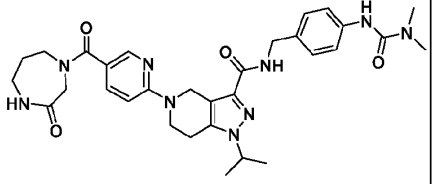
210	Ex. 193		5-(5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	570.4
211	Ex. 193		(*R*)-5-(5-(3-acetamidopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.5

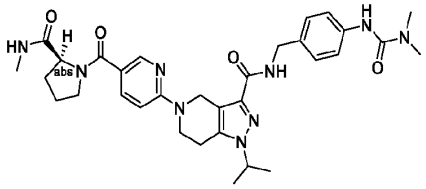
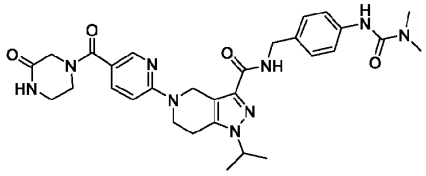
212	Ex. 193		5-(5-((1*R*,5*S*)-6-oxa-3-azabicyclo[3.1.1]heptane-3-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.4
213	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(ethyl(2-(methylamino)-2-oxoethyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	604.5

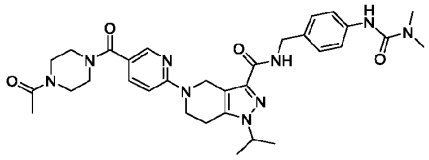
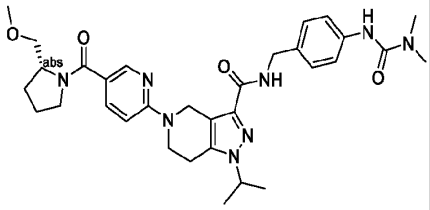
214	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-oxo-1,4-diazepane-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.4
215	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.4

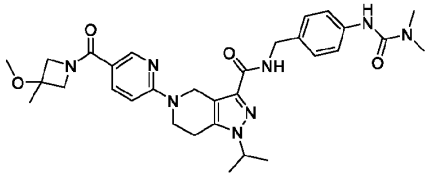
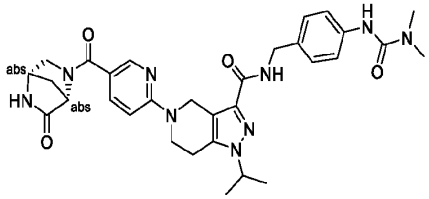
216	Ex. 193		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methoxypyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.5
217	Ex. 193		5-(5-(2,2-dimethyl-3-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.4

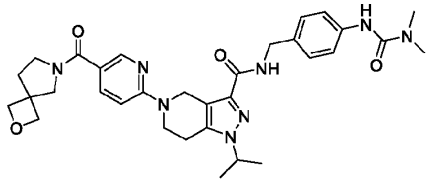
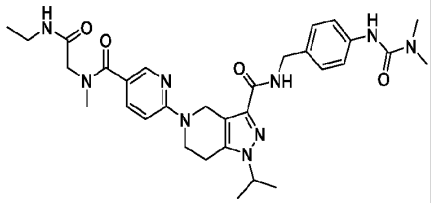
218	Ex. 193		(*R*)-5-(5-(2-carbamoylpyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.4
219	Ex. 193		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxy-3-methylpyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4

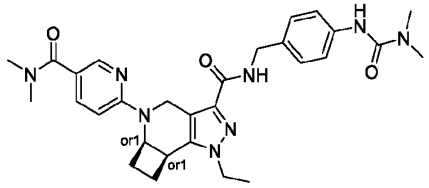
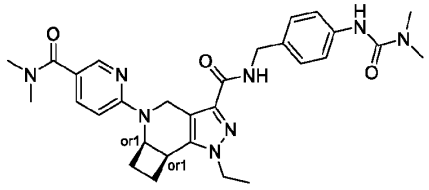
220	Ex. 193		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxypiperidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4
221	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxo-1,4-diazepane-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.4

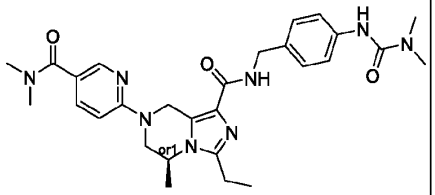
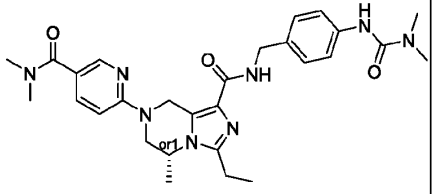
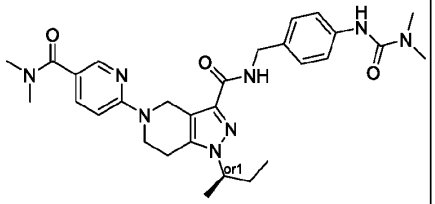
222	Ex. 193		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methylcarbamoyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.5
223	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxopiperazine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	588.4

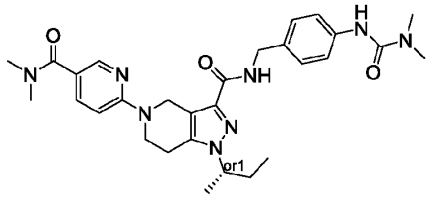
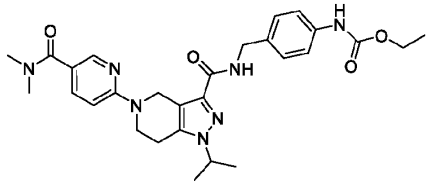
224	Ex. 193		5-(5-(4-acetylpiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.4
225	Ex. 193		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methoxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	603.5

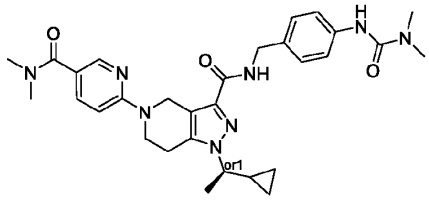
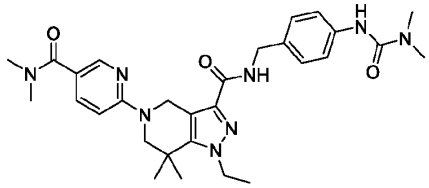
226	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methoxy-3-methylazetidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.4
227	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-((1*S*,4*S*)-6-oxo-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	600.7

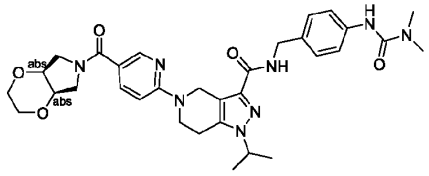
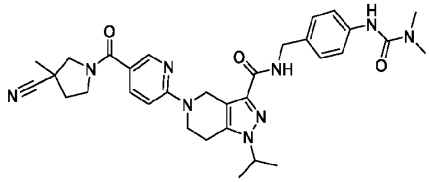
228	Ex. 193		5-(5-(2-oxa-6-azaspiro[3.4]octane-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.4
229	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((2-(ethylamino)-2-oxoethyl)(methyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	604.5

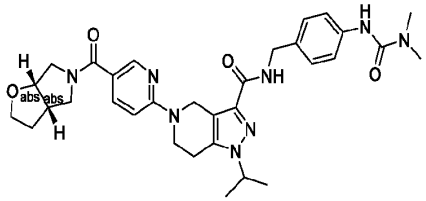
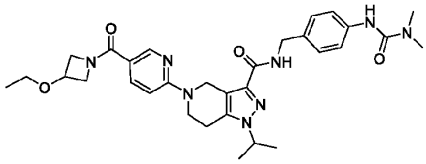
230 ^	Ex. 128		*rel*-(5*aR*,7*aS*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,5a,6,7,7a-hexahydro-1*H*-cyclobuta[*b*]pyrazolo[3,4-*d*]pyridine-3-carboxamide	545.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.51 (t, 1H), 8.28 (d, 1H), 8.24 (s, 1H), 7.68 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.22 – 7.18 (m, 2H), 6.89 (d, 1H), 5.53 (q, 1H), 5.33 (d, 1H), 4.42 – 4.30 (m, 2H), 4.24 (d, 1H), 4.12 – 3.99 (m, 2H), 3.77 (t, 1H), 2.99 (s, 6H), 2.92 (s, 6H), 2.32 – 2.22 (m, 1H), 2.21 – 2.07 (m, 2H), 1.65 (t, 1H), 1.38 (t, 3H).
231 ^	Ex. 128		*rel*-(5*aR*,7*aS*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,5*a*,6,7,7*a*-hexahydro-1*H*-cyclobuta[*b*]pyrazolo[3,4-*d*]pyridine-3-carboxamide	545.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.51 (t, 1H), 8.28 (d, 1H), 8.24 (s, 1H), 7.68 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.21 – 7.18 (m, 2H), 6.88 (d, 1H), 5.52 (q, 1H), 5.33 (d, 1H), 4.41 – 4.30 (m, 2H), 4.24 (d, 1H), 4.12 – 3.99 (m, 2H), 3.77 (t, 1H), 2.98 (s, 6H), 2.92 (s, 6H), 2.30 – 2.24 (m, 1H), 2.22 – 2.06 (m, 2H), 1.65 (t, 1H), 1.38 (t, 3H).

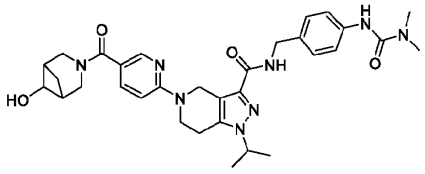
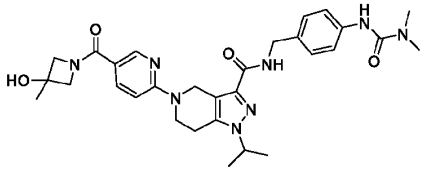
232 ^	Ex. 5		*rel-(R* or *S)*-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	533.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.32 (d, 1H), 7.75 (dd, 1H), 7.39 – 7.32 (m, 2H), 7.30 – 7.24 (m, 2H), 6.94 (d, 1H), 5.38 (d, 1H), 4.86 – 4.84 (m, 1H), 4.65 – 4.58 (m, 2H), 4.50 (s, 2H), 3.40 (dd, 1H), 3.11 (s, 6H), 3.01 (s, 6H), 2.86 – 2.66 (m, 2H), 1.43 – 1.33 (m, 6H).
233 ^	Ex. 5		*rel-(R* or *S)*-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	533.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.32 (d, 1H), 7.74 (dd, 1H), 7.39 – 7.32 (m, 2H), 7.31 – 7.25 (m, 2H), 6.93 (d, 1H), 5.38 (d, 1H), 4.86 – 4.84 (m, 1H), 4.66 – 4.55 (m, 2H), 4.50 (s, 2H), 3.44 – 3.36 (m, 1H), 3.11 (s, 6H), 3.01 (s, 6H), 2.81 – 2.67 (m, 2H), 1.42 – 1.32 (m, 6H).
234 ^	Ex. 43		*rel-(R* or *S)*-1-(*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.32 (t, 1H), 8.27 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.21 – 7.14 (m, 2H), 6.88 (d, 1H), 4.74 (s, 2H), 4.38 – 4.31 (m, 2H), 4.27 – 4.16 (m, 1H), 4.01 – 3.87 (m, 2H), 2.97 (s, 6H), 2.90 (s, 6H), 2.84 – 2.76 (m, 2H), 1.89 – 1.64 (m, 2H), 1.39 (d, 3H), 0.69 (t, 3H).

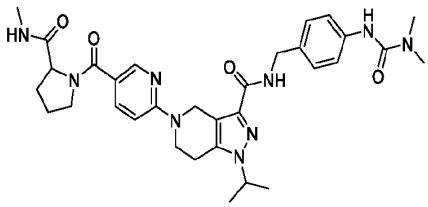
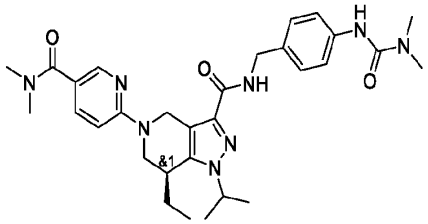
235 ^	Ex. 43		*rel-(R* or *S*)-1-(*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.35 – 8.28 (m, 1H), 8.26 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.21 – 7.14 (m, 2H), 6.88 (d, 1H), 4.79 – 4.68 (m, 2H), 4.40 – 4.29 (m, 2H), 4.27 – 4.17 (m, 1H), 4.02 – 3.88 (m, 2H), 3.81 – 3.73 (m, 1H), 2.97 (s, 6H), 2.91 (s, 6H), 2.83 – 2.75 (m, 2H), 1.92 – 1.65 (m, 1H), 1.41 – 1.35 (m, 3H), 0.70 (t, 3H).
236	Ex. 236		ethyl (4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate	534.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.46 (s, 1H), 8.28 (t, 1H), 8.16 – 8.14 (m, 1H), 7.55 (dd, 1H), 7.30 (d, 2H), 7.14 (d, 2H), 6.80 (d, 1H), 4.66 (s, 2H), 4.46 – 4.36 (m, 1H), 4.27 (d, 2H), 4.02 (q, 2H), 3.86 (t, 2H), 2.88 (s, 6H), 2.73 (t, 2H), 1.31 (d, 6H), 1.14 (t, 3H).

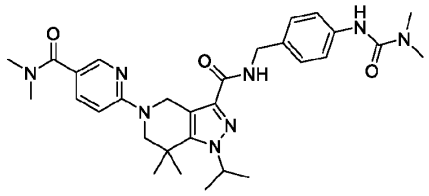
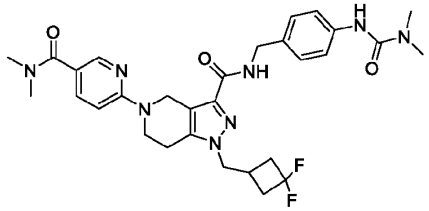
237 ^	Ex. 5		*rel-(R* or *S*)-1-(1-cyclopropylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 (d, 1H), 7.69 (dd, 1H), 7.37 – 7.33 (m, 2H), 7.32 – 7.27 (m, 2H), 6.91 (d, 1H), 4.84 – 4.70 (m, 2H), 4.52 (s, 2H), 4.20 – 4.09 (m, 1H), 4.06 – 3.96 (m, 1H), 3.71 – 3.60 (m, 1H), 3.10 (s, 6H), 3.02 (s, 6H), 2.84 (t, 2H), 1.58 (d, 3H), 1.46 – 1.36 (m, 1H), 0.71 – 0.60 (m, 1H), 0.51 – 0.39 (m, 1H), 0.38 – 0.24 (m, 2H).
238	Ex. 128		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.43 (t, 1H), 8.24 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.40 – 7.36 (m, 2H), 7.18 – 7.14 (m, 2H), 6.92 (d, 1H), 4.67 (s, 2H), 4.33 (d, 2H), 4.23 – 4.17 (m, 2H), 3.68 (s, 2H), 3.01 – 2.93 (m, 6H), 2.90 (s, 6H), 1.41 (t, 3H), 1.34 (s, 6H).

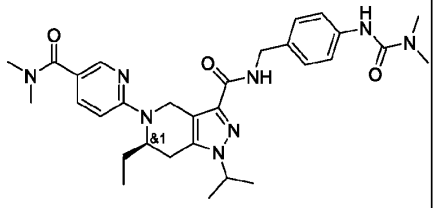
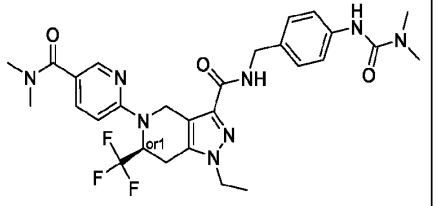
239	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4*aR*,7*aS*)-hexahydro-5*H*-[1,4]dioxino[2,3-*c*]pyrrole-6-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	617.8
240	Ex. 193		5-(5-(3-cyano-3-methylpyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	598.8

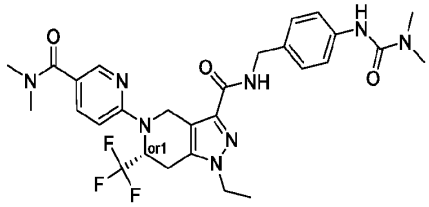
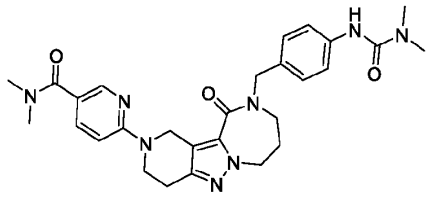
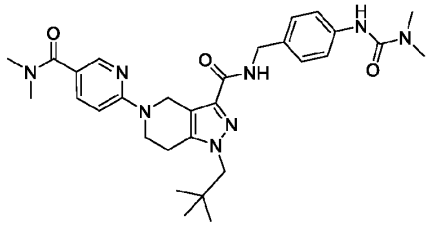
241	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((3*aS*,6*aS*)-hexahydro-2*H*-furo[2,3-*c*]pyrrole-5-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.7
242	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-ethoxyazetidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.8

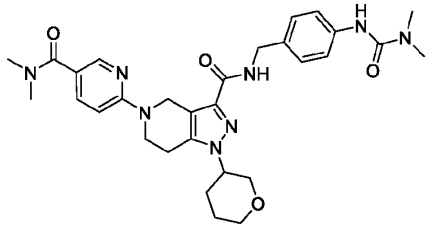
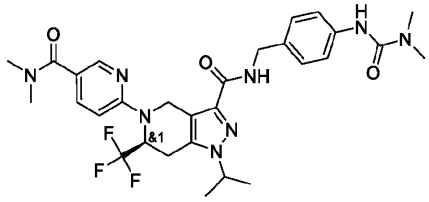
243	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(6-hydroxy-3-azabicyclo[3.1.1]heptane-3-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.7
244	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxy-3-methylazetidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.8

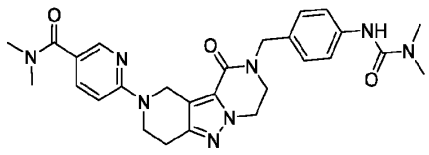
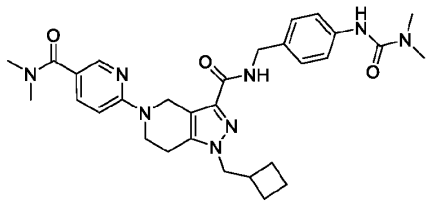
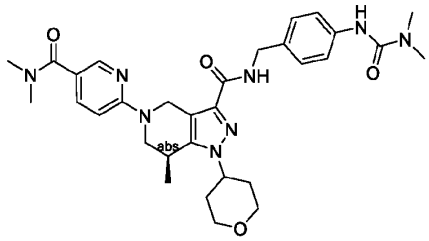
245	Ex. 193		*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methylcarbamoyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.8
246	Ex. 2[bd]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.36 (t, 1H), 8.26 – 8.20 (m, 2H), 7.67 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.21 – 7.14 (m, 2H), 6.85 (d, 1H), 5.04 – 4.98 (m, 1H), 4.81 (d, 1H), 4.56 – 4.48 (m, 1H), 4.39 – 4.29 (m, 2H), 4.21 (d, 1H), 3.19 – 3.12 (m, 1H), 3.04 – 2.94 (m, 6H), 2.92 – 2.89 (m, 6H), 1.57 – 1.51 (m, 1H), 1.48 – 1.37 (m, 8H), 1.06 – 1.00 (m, 3H).

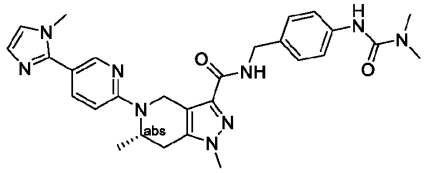
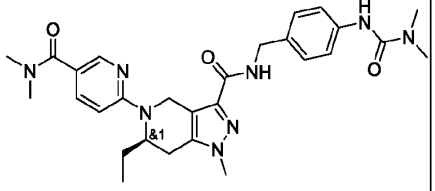
247	Ex. 125		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.5; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.37 (t, 1H), 8.24 – 8.19 (m, 2H), 7.67 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.19 – 7.14 (m, 2H), 6.98 (d, 1H), 4.74 – 4.67 (m, 3H), 4.35 (d, 2H), 3.69 (s, 2H), 2.97 (s, 6H), 2.90 (s, 6H), 1.43 (d, 6H), 1.35 (s, 6H).
248	Ex. 113		1-((3,3-difluorocyclobutyl)methyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	595.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.25 – 8.20 (m, 2H), 7.63 (dd, 1H), 7.40 – 7.35 (m, 2H), 7.18 – 7.13 (m, 2H), 6.88 (d, 1H), 4.74 (s, 2H), 4.33 (d, 2H), 4.16 (d, 2H), 3.94 (t, 2H), 2.96 (s, 6H), 2.90 (s, 6H), 2.80 (t, 2H), 2.69 – 2.58 (m, 3H), 2.47 – 2.38 (m, 2H).

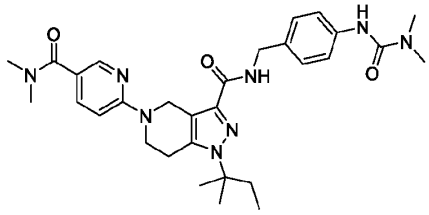
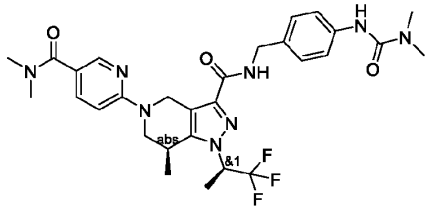
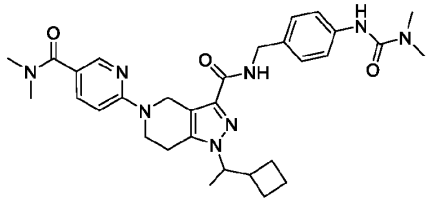
249	Ex. 128[de]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.2; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.34 (t, 1H), 8.26 – 8.19 (m, 2H), 7.65 (dd, 1H), 7.43 – 7.37 (m, 2H), 7.21 – 7.14 (m, 2H), 6.89 (d, 1H), 5.21 (d, 1H), 5.02 (s, 1H), 4.56 – 4.48 (m, 1H), 4.40 – 4.29 (m, 2H), 4.09 (d, 2H), 3.00 – 2.94 (m, 6H), 2.94 – 2.87 (m, 7H), 2.83 (d, 1H), 1.54 – 1.40 (m, 4H), 1.37 (d, 3H), 0.79 (t, 3H).
250 ^	Ex. 113[f]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.54 (t, 1H), 8.33 (d, 1H), 8.22 (s, 1H), 7.78 (dd, 1H), 7.40 – 7.36 (m, 2H), 7.20 – 7.16 (m, 2H), 7.02 (d, 1H), 6.31 – 6.21 (m, 1H), 5.05 (d, 1H), 4.38 – 4.06 (m, 5H), 3.30 – 3.14 (m, 2H), 2.98 (s, 6H), 2.90 (s, 6H), 1.33 (t, 3H).

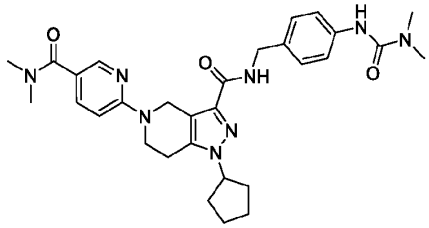
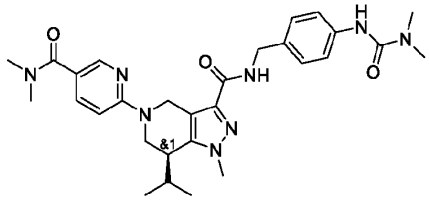
251 ^	Ex. 113[f]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.54 (t, 1H), 8.33 (d, 1H), 8.22 (s, 1H), 7.78 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 7.02 (d, 1H), 6.31 – 6.23 (m, 1H), 5.05 (d, 1H), 4.38 – 4.08 (m, 5H), 3.30 – 3.14 (m, 2H), 2.98 (s, 6H), 2.90 (s, 6H), 1.33 (t, 3H).
252	Ex. 252		6-(10-(4-(3,3-dimethylureido)benzyl)-11-oxo-1,3,4,7,8,9,10,11-octahydro-2*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepin-2-yl)-*N,N*-dimethylnicotinamide	531.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.28 (s, 1H), 8.24 (d, 1H), 7.64 (dd, 1H), 7.48 – 7.44 (m, 2H), 7.27 – 7.23 (m, 2H), 6.92 (d, 1H), 4.74 (s, 2H), 4.60 (s, 2H), 4.24 (t, 2H), 3.94 (t, 2H), 3.33 (t, 2H), 2.97 (s, 6H), 2.92 (s, 6H), 2.73 (t, 2H), 1.99 – 1.92 (m, 2H).
253	Ex. 113		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-neopentyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.32 (t, 1H), 8.26 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 6.89 (d, 1H), 4.74 (s, 2H), 4.35 (d, 2H), 3.94 (t, 2H), 3.83 (s, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.80 (t, 2H), 0.93 (s, 9H).

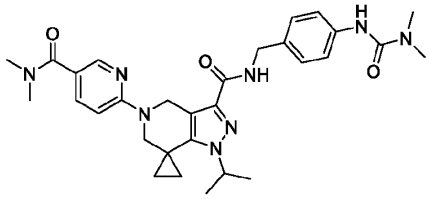
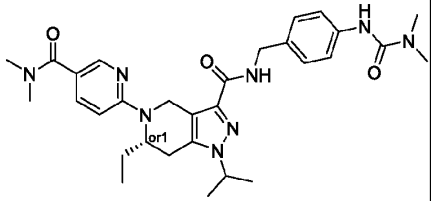
254	Ex. 113		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydro-2*H*-pyran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.37 (t, 1H), 8.23 – 8.21 (m, 2H), 7.62 (dd, 1H), 7.40 – 7.34 (m, 2H), 7.16 (d, 2H), 6.87 (d, 1H), 4.73 (s, 2H), 4.33 (d, 2H), 4.28 – 4.15 (m, 1H), 3.98 – 3.80 (m, 4H), 3.54 (t, 1H), 3.41 – 3.34 (m, 1H), 2.96 (s, 6H), 2.89 (s, 6H), 2.85 – 2.80 (m, 2H), 2.17 – 1.99 (m, 2H), 1.80 – 1.61 (m, 2H).
255	Ex. 113[df]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.2; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.42 (t, 1H), 8.33 (d, 1H), 8.23 (s, 1H), 7.78 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.22 – 7.14 (m, 2H), 7.03 – 6.98 (m, 1H), 6.32 – 6.22 (m, 1H), 5.04 (d, 1H), 4.68 – 4.57 (m, 1H), 4.40 – 4.23 (m, 3H), 3.31 – 3.19 (m, 2H), 2.98 (s, 6H), 2.91 (s, 6H), 1.41 (dd, 6H).

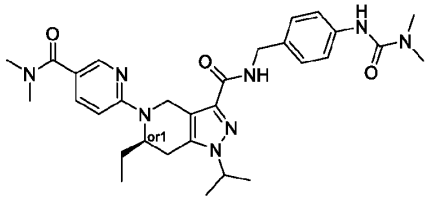
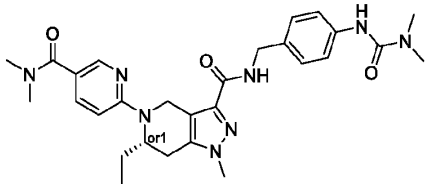
256	Ex. 252		6-(9-(4-(3,3-dimethylureido)benzyl)-10-oxo-3,4,7,8,9,10-hexahydropyrido[4',3':3,4]pyrazolo[1,5-*a*]pyrazin-2(1*H*)-yl)-*N*,*N*-dimethylnicotinamide	517.4
257	Ex. 113		1-(cyclobutylmethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.40 (t, 1H), 8.25 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 6.88 (d, 1H), 4.74 (s, 2H), 4.33 (d, 2H), 4.07 (d, 2H), 3.97 – 3.91 (m, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.84 – 2.68 (m, 3H), 2.00 – 1.90 (m, 2H), 1.87 – 1.69 (m, 4H).
258 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.43 (t, 1H), 8.26 – 8.20 (m, 2H), 7.63 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.17 (d, 2H), 6.89 (d, 1H), 5.09 (d, 1H), 4.50 – 4.17 (m, 5H), 4.01 – 3.91 (m, 2H), 3.56 – 3.46 (m, 2H), 3.31 – 3.19 (m, 2H), 2.97 (s, 6H), 2.90 (s, 6H), 2.23 – 2.02 (m, 2H), 1.86 – 1.73 (m, 2H), 1.24 – 1.17 (m, 3H).

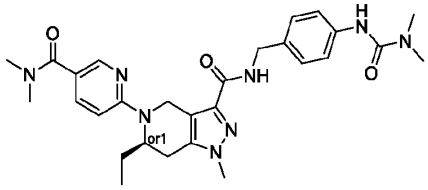
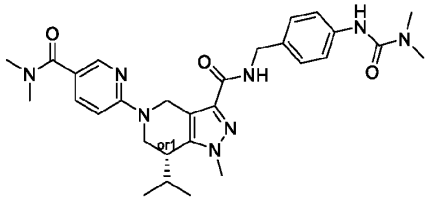
259	Ex. 42		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.3; ^{1}H NMR* (400 MHz, CD_3OD) δ 8.49 – 8.36 (m, 2H), 7.83 (dd, 1H), 7.37 – 7.32 (m, 2H), 7.31 – 7.26 (m, 3H), 7.18 (d, 1H), 6.98 (d, 1H), 5.56 – 5.45 (m, 1H), 5.11 (d, 1H), 4.55 – 4.48 (m, 2H), 4.28 (d, 1H), 3.84 – 3.78 (m, 6H), 3.07 – 2.99 (m, 7H), 2.75 (d, 1H), 1.17 (d, 3H).
260	Ex. 113		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.49 (t, 1H), 8.26 – 8.20 (m, 2H), 7.63 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 6.87 (d, 1H), 5.30 – 5.20 (m, 1H), 5.06 – 4.95 (m, 1H), 4.39 – 4.25 (m, 2H), 4.05 (d, 1H), 3.80 – 3.70 (m, 3H), 2.98 (s, 6H), 2.93 – 2.85 (m, 7H), 2.82 – 2.72 (m, 1H), 1.58 – 1.39 (m, 2H), 0.81 (t, 3H).

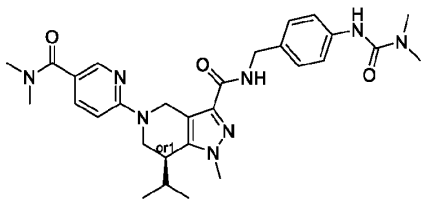
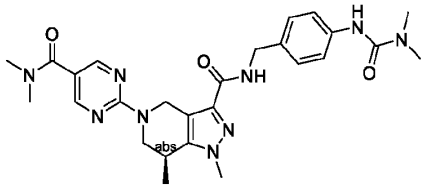
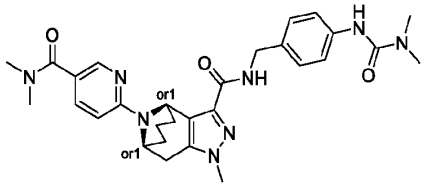
261	Ex. 9		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(*tert*-pentyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.22 (s, 1H), 8.16 (d, 1H), 7.42 – 7.35 (m, 2H), 7.17 (d, 2H), 6.75 (s, 1H), 6.56 (d, 1H), 4.67 (s, 2H), 4.34 (d, 2H), 3.87 (t, 2H), 3.00 – 2.93 (m, 6H), 2.90 (s, 6H), 2.85 (s, 2H), 1.87 (q, 2H), 1.55 (s, 6H), 0.64 (t, 3H).
262 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-((*RS*)-1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, 1H), 7.67 – 7.62 (m, 1H), 7.39 – 7.34 (m, 2H), 7.31 – 7.28 (m, 2H), 7.14 (t, 1H), 6.78 (d, 1H), 6.31 (s, 1H), 5.01 (d, 1H), 4.92 – 4.85 (m, 1H), 4.70 – 4.57 (m, 2H), 4.53 – 4.37 (m, 2H), 3.36 – 3.28 (m, 1H), 3.16 – 3.07 (m, 8H), 3.05 – 3.01 (m, 6H), 1.78 (d, 3H), 1.26 (d, 3H).
263	Ex. 113		1-(1-cyclobutylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.31 (t, 1H), 8.26 – 8.19 (m, 2H), 7.64 (dd, 1H), 7.43 – 7.34 (m, 2H), 7.18 (d, 2H), 6.88 (d, 1H), 4.79 – 4.60 (m, 2H), 4.39 – 4.20 (m, 3H), 4.04 – 3.86 (m, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.86 – 2.73 (m, 3H), 2.08 – 1.96 (m, 1H), 1.82 – 1.56 (m, 5H), 1.29 (d, 3H).

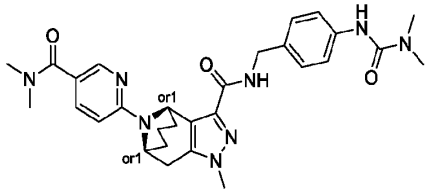
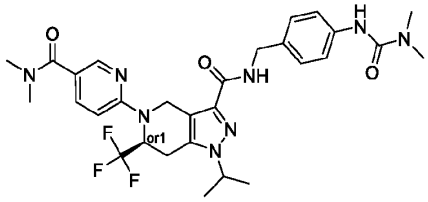
264	Ex. 113		1-cyclopentyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.25 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 6.89 (d, 1H), 4.75 (s, 2H), 4.71 – 4.57 (m, 1H), 4.35 (d, 2H), 3.95 (t, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.85 – 2.78 (m, 2H), 2.09 – 1.90 (m, 4H), 1.87 – 1.78 (m, 2H), 1.66 – 1.56 (m, 2H).
265	Ex. 113		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-isopropyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.57 – 8.48 (m, 1H), 8.32 – 8.18 (m, 2H), 7.71 – 7.63 (m, 1H), 7.44 – 7.34 (m, 2H), 7.22 – 7.12 (m, 2H), 6.83 – 6.74 (m, 1H), 5.02 – 4.78 (m, 2H), 4.42 – 4.24 (m, 3H), 3.86 – 3.79 (m, 3H), 3.12 – 2.95 (m, 8H), 2.94 – 2.87 (m, 6H), 1.96 – 1.83 (m, 1H), 1.05 – 0.95 (m, 3H), 0.91 – 0.82 (m, 3H).

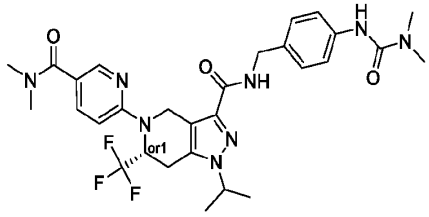
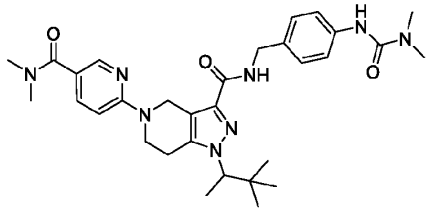
266	Ex. 127		5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-isopropyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide	559.6; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.23 (s, 1H), 8.21 – 8.20 (m, 1H), 7.65 – 7.61 (m, 1H), 7.42 – 7.37 (m, 2H), 7.20 – 7.15 (m, 2H), 6.90 (d, 1H), 4.81 (s, 2H), 4.35 (d, 2H), 3.98 – 3.90 (m, 1H), 3.73 (s, 2H), 3.03 – 2.93 (m, 6H), 2.91 (s, 6H), 1.38 (d, 6H), 1.30 (t, 2H), 1.09 (t, 2H).
267 ^	Ex. 128[de]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.34 (t, 1H), 8.26 – 8.21 (m, 2H), 7.63 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.21 – 7.15 (m, 2H), 6.86 (d, 1H), 5.22 (d, 1H), 5.03 (s, 1H), 4.58 – 4.46 (m, 1H), 4.40 – 4.26 (m, 2H), 4.07 (d, 1H), 3.03 – 2.94 (m, 6H), 2.93 – 2.88 (m, 7H), 2.86 – 2.78 (m, 1H), 1.56 – 1.35 (m, 8H), 0.79 (t, 3H).

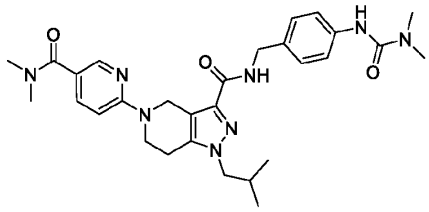
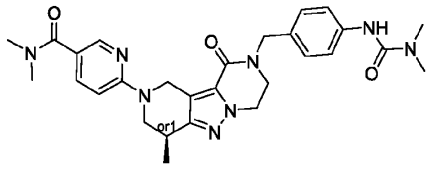
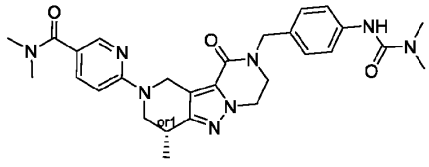
268 ^	Ex. 128[de]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.2
269 ^	Ex. 113		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.58 – 8.44 (m, 1H), 8.32 – 8.20 (m, 2H), 7.73 – 7.60 (m, 1H), 7.47 – 7.34 (m, 2H), 7.24 – 7.11 (m, 2H), 6.94 – 6.83 (m, 1H), 5.38 – 5.19 (m, 1H), 5.09 – 4.92 (m, 1H), 4.40 – 4.26 (m, 2H), 4.13 – 3.98 (m, 1H), 3.84 – 3.71 (m, 3H), 3.06 – 2.97 (m, 6H), 2.94 – 2.89 (m, 6H), 2.89 – 2.65 (m, 2H), 1.59 – 1.40 (m, 2H), 0.89 – 0.77 (m, 3H).

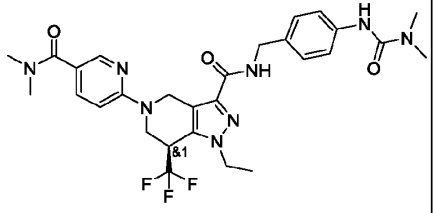
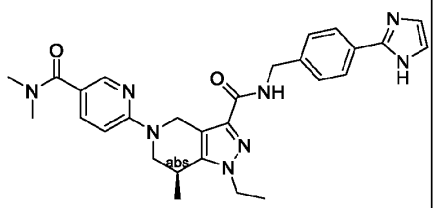
270 ^	Ex. 113		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.49 (t, 1H), 8.27 – 8.19 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.17 (d, 2H), 6.87 (d, 1H), 5.32 – 5.20 (m, 1H), 5.08 – 4.92 (m, 1H), 4.40 – 4.25 (m, 2H), 4.05 (d, 1H), 3.77 (s, 3H), 2.98 (s, 6H), 2.93 – 2.85 (m, 7H), 2.82 – 2.74 (m, 1H), 1.59 – 1.40 (m, 2H), 0.81 (t, 3H).
271 ^	Ex. 113		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-isopropyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.53 (t, 1H), 8.28 (d, 1H), 8.22 (s, 1H), 7.67 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.20 – 7.14 (m, 2H), 6.79 (d, 1H), 4.99 – 4.79 (m, 2H), 4.40 – 4.25 (m, 3H), 3.84 (s, 3H), 3.11 – 3.03 (m, 1H), 2.99 (s, 6H), 2.96 – 2.92 (m, 1H), 2.91 – 2.88 (m, 6H), 1.95 – 1.80 (m, 1H), 1.00 (d, 3H), 0.88 (d, 3H).

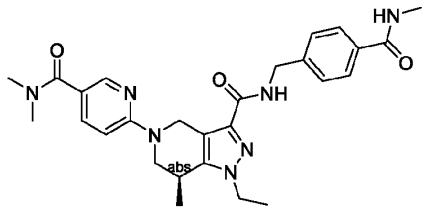
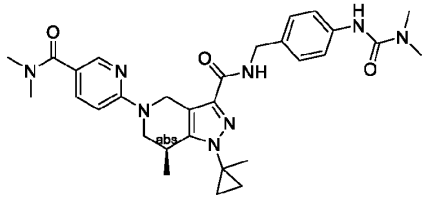
272 ^	Ex. 113		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-isopropyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.53 (t, 1H), 8.28 (d, 1H), 8.22 (s, 1H), 7.67 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.21 – 7.13 (m, 2H), 6.79 (d, 1H), 5.02 – 4.80 (m, 2H), 4.41 – 4.25 (m, 3H), 3.84 (s, 3H), 3.12 – 3.03 (m, 1H), 2.99 (s, 6H), 2.95 – 2.92 (m, 1H), 2.91 – 2.88 (m, 6H), 1.96 – 1.84 (m, 1H), 1.00 (d, 3H), 0.88 (d, 3H).
273 ^	Ex. 77		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	520.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.56 – 8.44 (m, 3H), 8.22 (s, 1H), 7.42 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 5.40 (d, 1H), 4.63 (dd, 1H), 4.47 – 4.25 (m, 3H), 3.82 (s, 3H), 3.51 (dd, 1H), 3.27 – 3.19 (m, 1H), 3.05 – 2.95 (m, 6H), 2.91 (s, 6H), 1.16 (d, 3H).
274 ^	Ex. 5		*rel*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxamide	545.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.22 (d, 1H), 7.64 – 7.56 (m, 1H), 7.36 – 7.29 (m, 2H), 7.28 – 7.22 (m, 2H), 6.86 (d, 1H), 5.90 – 5.84 (m, 1H), 5.22 – 5.15 (m, 1H), 4.47 (s, 2H), 3.77 – 3.69 (m, 3H), 3.16 – 2.97 (m, 13H), 2.69 – 2.56 (m, 1H), 1.97 – 1.76 (m, 4H), 1.58 – 1.34 (m, 2H).

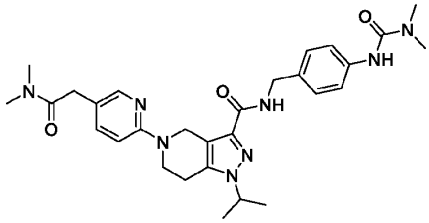
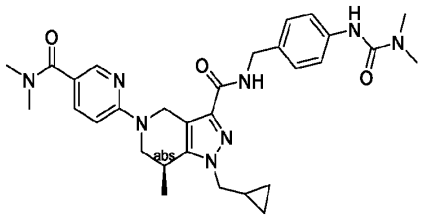
275 ^	Ex. 5		*rel*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxamide	545.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.23 (d, 1H), 7.62 – 7.58 (m, 1H), 7.35 – 7.30 (m, 2H), 7.28 – 7.23 (m, 2H), 6.86 (d, 1H), 5.87 (s, 1H), 5.24 – 5.13 (m, 1H), 4.47 (s, 2H), 3.74 – 3.72 (m, 3H), 3.17 – 2.96 (m, 13H), 2.63 (d, 1H), 1.97 – 1.75 (m, 4H), 1.60 – 1.35 (m, 2H).
276 ^	Ex. 113[df]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.42 (t, 1H), 8.33 (d, 1H), 8.23 (s, 1H), 7.78 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.21 – 7.16 (m, 2H), 7.01 (d, 1H), 6.31 – 6.22 (m, 1H), 5.04 (d, 1H), 4.65 – 4.56 (m, 1H), 4.39 – 4.23 (m, 3H), 3.29 – 3.19 (m, 2H), 3.03 – 2.95 (m, 6H), 2.90 (s, 6H), 1.41 (dd, 6H).

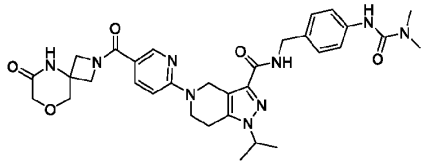
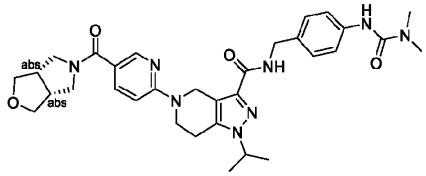
277 ^	Ex. 113[df]		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.42 (t, 1H), 8.33 – 8.32 (m, 1H), 8.23 (s, 1H), 7.78 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.21 – 7.17 (m, 2H), 7.01 (d, 1H), 6.32 – 6.21 (m, 1H), 5.04 (d, 1H), 4.66 – 4.57 (m, 1H), 4.39 – 4.24 (m, 3H), 3.31 – 3.19 (m, 2H), 3.03 – 2.96 (m, 6H), 2.90 (s, 6H), 1.41 (dd, 6H).
278	Ex. 113		1-(3,3-dimethylbutan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	575.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.30 – 8.19 (m, 3H), 7.64 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.21 – 7.15 (m, 2H), 6.88 (d, 1H), 4.85 – 4.60 (m, 2H), 4.44 – 4.27 (m, 2H), 4.13 – 3.99 (m, 2H), 3.85 – 3.76 (m, 1H), 2.97 (s, 6H), 2.91 (s, 6H), 2.84 – 2.75 (m, 2H), 1.41 (d, 3H), 0.89 (s, 9H).

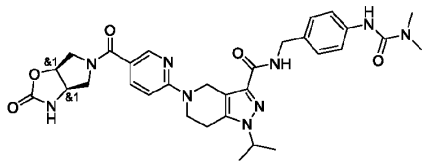
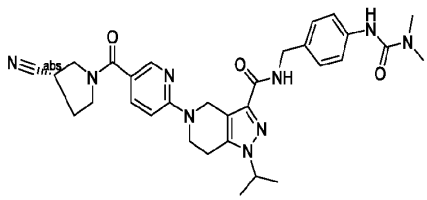
279	Ex. 43		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isobutyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.42 (t, 1H), 8.25 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.20 – 7.14 (m, 2H), 6.88 (d, 1H), 4.74 (s, 2H), 4.33 (d, 2H), 3.95 (t, 2H), 3.85 (d, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.83 – 2.74 (m, 2H), 2.22 – 2.05 (m, 1H), 0.85 (d, 6H).
280 ^	Ex. 252		*rel-(R* or *S*)-6-(9-(4-(3,3-dimethylureido)benzyl)-4-methyl-10-oxo-3,4,7,8,9,10-hexahydropyrido[4',3':3,4]pyrazolo[1,5-*a*]pyrazin-2(1*H*)-yl)-*N,N*-dimethylnicotinamide	531.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.28 (s, 1H), 8.25 – 8.24 (m, 1H), 7.64 (dd, 1H), 7.46 – 7.42 (m, 2H), 7.21 – 7.17 (m, 2H), 6.93 (d, 1H), 5.08 (d, 1H), 4.69 – 4.47 (m, 3H), 4.34 – 4.20 (m, 3H), 3.67 (t, 2H), 3.31 – 3.25 (m, 1H), 3.04 – 2.94 (m, 7H), 2.91 (s, 6H), 1.25 (d, 3H).
281 ^	Ex. 252		*rel-(R* or *S*)-6-(9-(4-(3,3-dimethylureido)benzyl)-4-methyl-10-oxo-3,4,7,8,9,10-hexahydropyrido[4',3':3,4]pyrazolo[1,5-*a*]pyrazin-2(1*H*)-yl)-*N,N*-dimethylnicotinamide	531.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.28 (s, 1H), 8.25 (d, 1H), 7.64 (dd, 1H), 7.46 – 7.42 (m, 2H), 7.21 – 7.17 (m, 2H), 6.93 (d, 1H), 5.08 (d, 1H), 4.67 – 4.49 (m, 3H), 4.34 – 4.19 (m, 3H), 3.67 (t, 2H), 3.31 – 3.25 (m, 1H), 3.04 – 2.95 (m, 7H), 2.91 (d, 6H), 1.25 (d, 3H).

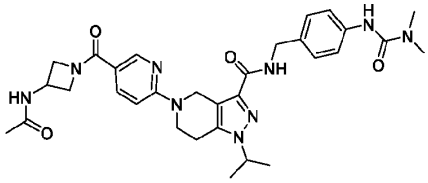
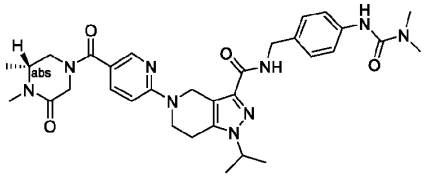
282	Ex. 3[l]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.4; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.62 (t, 1H), 8.28 – 8.27 (m, 1H), 8.22 (s, 1H), 7.69 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.20 – 7.15 (m, 2H), 6.84 (d, 1H), 5.27 (d, 1H), 5.08 (d, 1H), 4.51 – 4.42 (m, 1H), 4.40 – 4.11 (m, 5H), 3.32 – 3.26 (m, 1H), 3.03 – 2.94 (m, 6H), 2.90 (s, 6H), 1.42 (t, 3H).
283	Ex. 125		(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	513.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 14.66 (s, 1H), 8.74 (t, 1H), 8.25 – 8.20 (m, 1H), 7.98 – 7.92 (m, 2H), 7.82 (s, 2H), 7.64 (dd, 1H), 7.58 – 7.55 (m, 2H), 6.91 (d, 1H), 5.06 (d, 1H), 4.58 – 4.42 (m, 2H), 4.37 – 4.22 (m, 2H), 4.19 – 4.07 (m, 2H), 3.41 (dd, 1H), 3.27 – 3.21 (m, 1H), 3.01 – 2.94 (m, 6H), 1.41 (t, 3H), 1.21 (d, 3H).

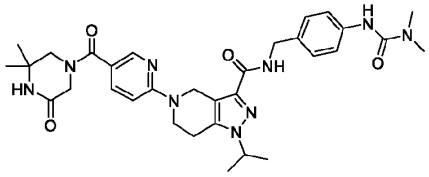
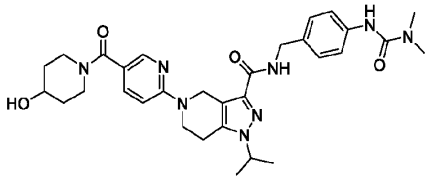
284	Ex. 125		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	504.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.66 (t, 1H), 8.36 (q, 1H), 8.22 (d, 1H), 7.79 – 7.75 (m, 2H), 7.69 – 7.64 (m, 1H), 7.39 – 7.34 (m, 2H), 6.95 (d, 1H), 5.04 (d, 1H), 4.51 – 4.38 (m, 2H), 4.37 – 4.27 (m, 2H), 4.19 – 4.05 (m, 2H), 3.42 (dd, 1H), 3.27 – 3.20 (m, 1H), 3.00 – 2.94 (m, 6H), 2.77 (d, 3H), 1.40 (t, 3H), 1.21 (d, 3H).
285 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.46 (t, 1H), 8.27 – 8.19 (m, 2H), 7.64 (dd, 1H), 7.43 – 7.33 (m, 2H), 7.21 - 7.15 (m, 2H), 6.91 – 6.86 (m, 1H), 4.78 (d, 1H), 4.57 (d, 1H), 4.40 – 4.24 (m, 2H), 4.01 (dd, 1H), 3.67 (dd, 1H), 2.98 (s, 6H), 2.91 (s, 6H), 1.54 (s, 3H), 1.50 – 1.42 (m, 1H), 1.35 (d, 3H), 1.32 – 1.22 (m, 2H), 1.12 – 1.07 (m, 1H), 1.02 – 0.97 (m, 1H).

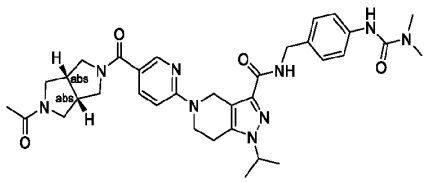
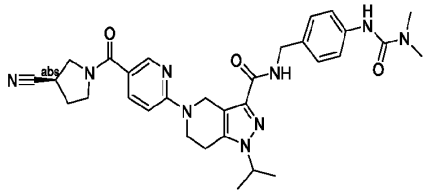
286	Ex. 286		5-(5-(2-(dimethylamino)-2-oxoethyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 – 8.16 (m, 2H), 7.91 (s, 1H), 7.35 (d, 3H), 7.14 (d, 2H), 6.79 (d, 1H), 4.60 (s, 2H), 4.50 – 4.37 (m, 1H), 4.35 – 4.27 (m, 2H), 3.89 – 3.76 (m, 2H), 3.53 – 3.44 (m, 2H), 2.97 (s, 3H), 2.87 (s, 6H), 2.80 – 2.70 (m, 5H), 1.35 (d, 6H).
287 ^	Ex. 113		(*S*)-1-(cyclopropylmethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.44 – 8.35 (m, 1H), 8.23 – 8.16 (m, 2H), 7.64 – 7.57 (m, 1H), 7.34 (d, 2H), 7.13 (d, 2H), 6.85 (d, 1H), 5.02 (d, 1H), 4.43 – 4.19 (m, 4H), 4.07 – 3.97 (m, 1H), 3.88 – 3.77 (m, 1H), 3.24 – 3.14 (m, 2H), 2.94 (s, 6H), 2.86 (s, 6H), 1.30 – 1.12 (m, 4H), 0.53 – 0.43 (m, 2H), 0.40 – 0.32 (m, 2H).

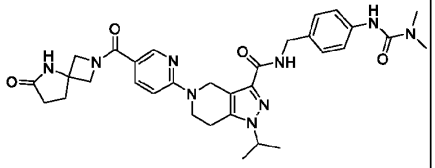
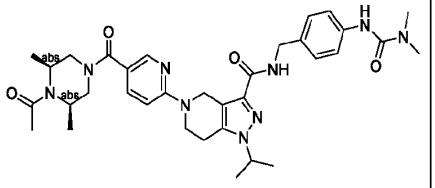
288	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-8-oxa-2,5-diazaspiro[3.5]nonane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	630.6
289	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((3*aR*,6*aS*)-hexahydro-1*H*-furo[3,4-*c*]pyrrole-5-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.7

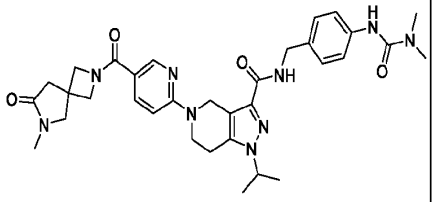
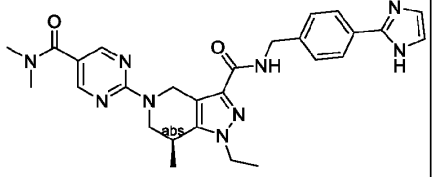
290	Ex. 193		*rac-N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-((3*aR*,6*aS*)-2-oxohexahydro-2*H*-pyrrolo[3,4-*d*]oxazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.6
291	Ex. 193		(*S*)-5-(5-(3-cyanopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	584.6

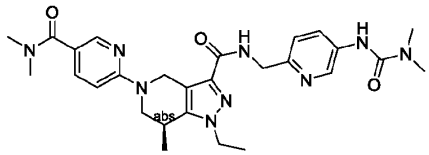
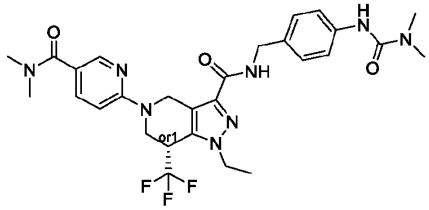
292	Ex. 193		5-(5-(3-acetamidoazetidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.6
293	Ex. 193		(*R*)-5-(5-(3,4-dimethyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.6

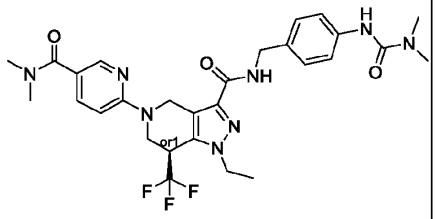
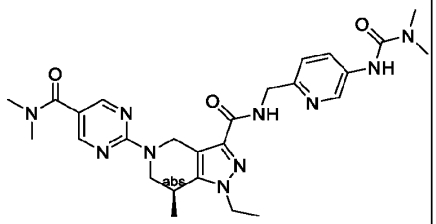
294	Ex. 193		5-(5-(3,3-dimethyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.6
295	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-hydroxypiperidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.6

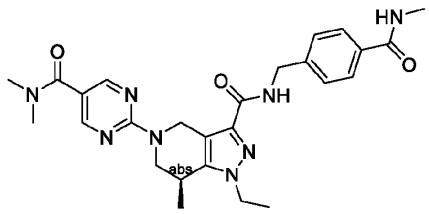
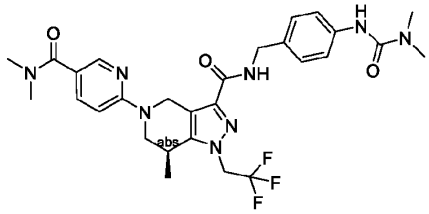
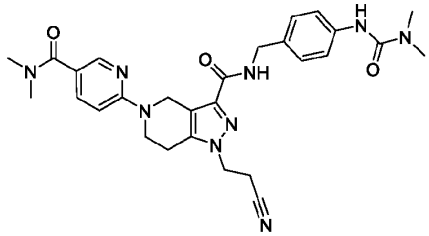
296	Ex. 193		5-(5-((3*aR*,6*aS*)-5-acetyloctahydropyrrolo[3,4-*c*]pyrrole-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.6
297	Ex. 193		(*R*)-5-(5-(3-cyanopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	584.6

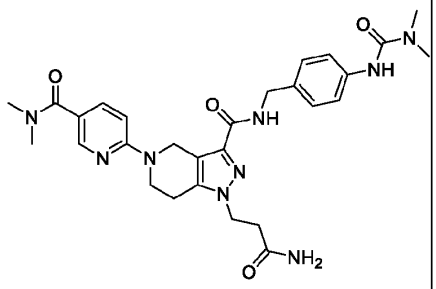
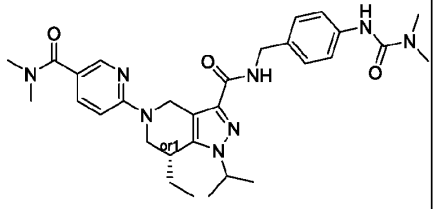
298	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-2,5-diazaspiro[3.4]octane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	614.6
299	Ex. 193		5-(5-((3*S*,5*R*)-4-acetyl-3,5-dimethylpiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	644.7

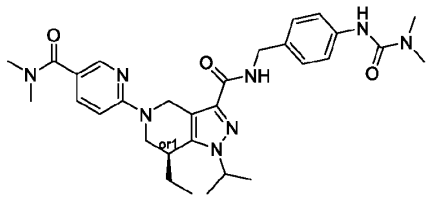
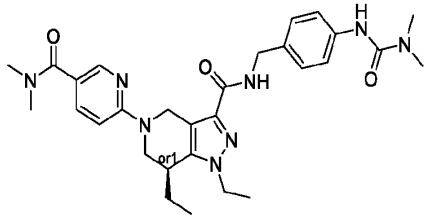
300	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-methyl-7-oxo-2,6-diazaspiro[3.4]octane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	628.6
301	Ex. 125		(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	514.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 14.70 (s, 1H), 8.74 (t, 1H), 8.51 (s, 2H), 7.97 – 7.93 (m, 2H), 7.79 – 7.78 (m, 2H), 7.57 – 7.54 (m, 2H), 5.40 (d, 1H), 4.68 (dd, 1H), 4.55 – 4.43 (m, 2H), 4.40 – 4.35 (m, 1H), 4.20 – 4.04 (m, 2H), 3.48 (dd, 1H), 3.29 – 3.22 (m, 1H), 3.06 – 2.91 (m, 6H), 1.40 (t, 3H), 1.17 (d, 3H).

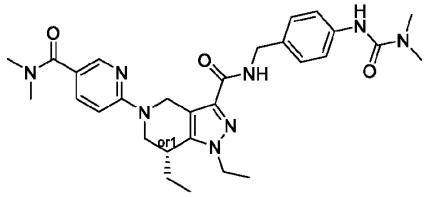
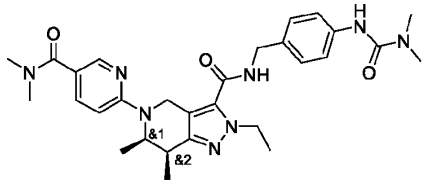
302	Ex. 126		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	534.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.96 – 8.90 (m, 1H), 8.84 – 8.80 (m, 1H), 8.75 – 8.71 (m, 1H), 8.24 – 8.17 (m, 2H), 7.65 (dd, 1H), 7.59 (s, 1H), 6.92 (d, 1H), 5.05 (d, 1H), 4.64 – 4.52 (m, 2H), 4.37 – 4.25 (m, 2H), 4.20 – 4.07 (m, 2H), 3.41 (dd, 1H), 3.28 – 3.21 (m, 1H), 3.00 – 2.97 (m, 6H), 2.96 – 2.92 (m, 6H), 1.41 (t, 3H), 1.22 (d, 3H).
303 ^	Ex. 3^l		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.63 (t, 1H), 8.28 (d, 1H), 8.24 (s, 1H), 7.70 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.21 – 7.16 (m, 2H), 6.85 (d, 1H), 5.28 (d, 1H), 5.09 (d, 1H), 4.52 – 4.46 (m, 1H), 4.41 – 4.32 (m, 2H), 4.31 – 4.26 (m, 1H), 4.24 – 4.14 (m, 2H), 3.31 – 3.27 (m, 1H), 3.04 – 2.96 (m, 6H), 2.91 (s, 6H), 1.43 (t, 3H).

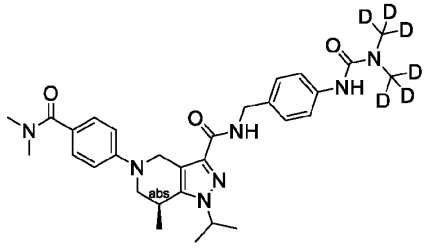
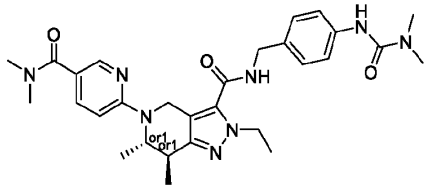
304 ^	Ex. 3[l]		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.62 (t, 1H), 8.28 – 8.26 (m, 1H), 8.23 (s, 1H), 7.69 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.20 – 7.16 (m, 2H), 6.84 (d, 1H), 5.27 (d, 1H), 5.08 (d, 1H), 4.51 – 4.45 (m, 1H), 4.39 – 4.31 (m, 2H), 4.30 – 4.24 (m, 1H), 4.23 – 4.13 (m, 2H), 3.30 – 3.26 (m, 1H), 3.03 – 2.94 (m, 6H), 2.90 (s, 6H), 1.42 (t, 3H).
305	Ex. 125		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	535.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.94 – 8.80 (m, 1H), 8.77 (s, 1H), 8.70 – 8.64 (m, 1H), 8.57 – 8.49 (m, 2H), 8.16 – 8.10 (m, 1H), 7.54 – 7.48 (m, 1H), 5.41 (d, 1H), 4.68 (dd, 1H), 4.64 – 4.49 (m, 2H), 4.37 (d, 1H), 4.19 – 4.07 (m, 2H), 3.48 (dd, 1H), 3.30 – 3.23 (m, 1H), 3.05 – 2.97 (m, 6H), 2.96 – 2.92 (m, 6H), 1.44 – 1.38 (m, 3H), 1.17 (d, 3H).

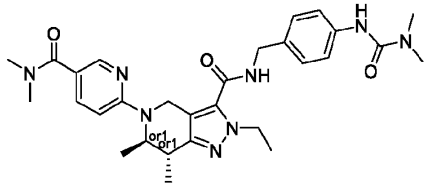
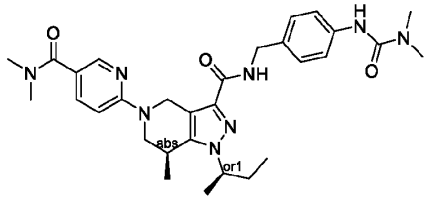
306	Ex. 125		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	505.4; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.65 (t, 1H), 8.51 (s, 2H), 8.36 (q, 1H), 7.79 – 7.75 (m, 2H), 7.38 – 7.34 (m, 2H), 5.40 (d, 1H), 4.67 (dd, 1H), 4.51 – 4.34 (m, 3H), 4.17 – 4.05 (m, 2H), 3.48 (dd, 1H), 3.28 – 3.22 (m, 1H), 3.03 – 2.96 (m, 6H), 2.77 (d, 3H), 1.39 (t, 3H), 1.16 (d, 3H).
307 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.50 (t, 1H), 8.26 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.40 – 7.35 (m, 2H), 7.19 – 7.14 (m, 2H), 6.91 (d, 1H), 5.23 – 5.03 (m, 3H), 4.52 – 4.21 (m, 4H), 3.29 – 3.21 (m, 2H), 2.98 (s, 6H), 2.90 (s, 6H), 1.20 (d, 3H).
308	Ex. 39		1-(2-cyanoethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	544.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.48 – 8.41 (m, 1H), 8.26 – 8.21 (m, 2H), 7.67 – 7.61 (m, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 6.93 – 6.88 (m, 1H), 4.76 (s, 2H), 4.38 – 4.31 (m, 4H), 3.99 – 3.92 (m, 2H), 3.09 – 3.04 (m, 2H), 2.97 (s, 6H), 2.91 (s, 8H).

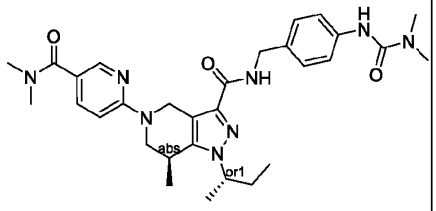
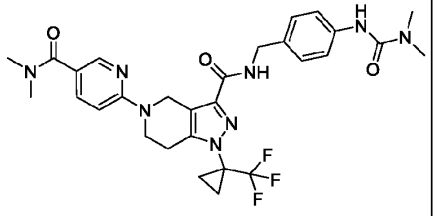
309	Ex. 39		1-(3-amino-3-oxopropyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	562.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.41 (t, 1H), 8.25 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.41 – 7.34 (m, 3H), 7.20 – 7.14 (m, 2H), 6.93 – 6.85 (m, 2H), 4.74 (s, 2H), 4.34 (d, 2H), 4.21 (t, 2H), 3.97 – 3.90 (m, 2H), 2.99 – 2.95 (m, 6H), 2.91 (s, 6H), 2.86 – 2.81 (m, 2H), 2.62 (t, 2H).
310 ^	Ex. 2[bd]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.38 – 8.33 (m, 1H), 8.27 – 8.21 (m, 2H), 7.67 – 7.63 (m, 1H), 7.42 – 7.37 (m, 2H), 7.21 – 7.16 (m, 2H), 6.84 – 6.81 (m, 1H), 5.02 (d, 1H), 4.82 (d, 1H), 4.57 – 4.48 (m, 1H), 4.40 – 4.29 (m, 2H), 4.20 (d, 1H), 3.18 – 3.11 (m, 1H), 3.02 – 2.96 (m, 7H), 2.92 – 2.89 (m, 6H), 1.58 – 1.50 (m, 1H), 1.48 – 1.41 (m, 4H), 1.40 – 1.37 (m, 3H), 1.07 – 1.02 (m, 3H).

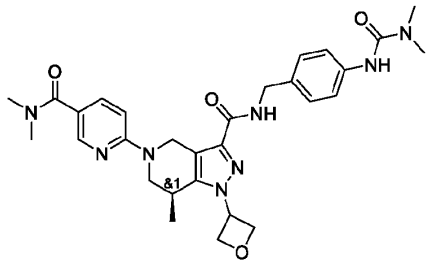
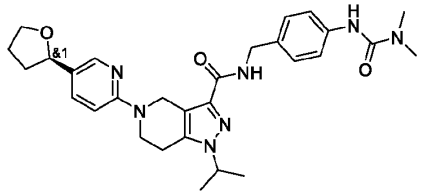
311 ^	Ex. 2[bd]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.26 – 8.25 (m, 1H), 8.22 (s, 1H), 7.65 (dd, 1H), 7.41 – 7.37 (m, 2H), 7.20 – 7.15 (m, 2H), 6.82 (d, 1H), 5.02 (d, 1H), 4.82 (d, 1H), 4.56 – 4.48 (m, 1H), 4.39 – 4.30 (m, 2H), 4.22 – 4.17 (m, 1H), 3.20 – 3.09 (m, 1H), 3.03 – 2.94 (m, 7H), 2.90 (s, 6H), 1.58 – 1.49 (m, 1H), 1.48 – 1.41 (m, 4H), 1.40 – 1.37 (m, 3H), 1.04 (t, 3H).
312 ^	Ex. 113[d]		*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.26 – 8.24 (m, 1H), 8.22 (s, 1H), 7.67 – 7.63 (m, 1H), 7.40 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 6.83 (d, 1H), 5.00 (d, 1H), 4.77 (d, 1H), 4.38 – 4.29 (m, 2H), 4.26 – 4.19 (m, 1H), 4.16 – 4.03 (m, 2H), 3.20 – 3.12 (m, 1H), 3.03 – 2.93 (m, 7H), 2.90 (s, 6H), 1.61 – 1.53 (m, 1H), 1.47 – 1.37 (m, 4H), 1.03 (t, 3H).

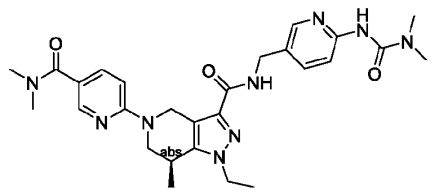
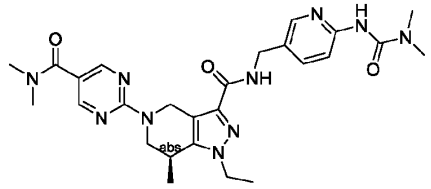
313 ^	Ex. 113[d]		*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.45 (t, 1H), 8.26 – 8.24 (m, 1H), 8.22 (s, 1H), 7.65 (dd, 1H), 7.40 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 6.83 (d, 1H), 5.00 (d, 1H), 4.77 (d, 1H), 4.38 – 4.28 (m, 2H), 4.26 – 4.19 (m, 1H), 4.15 – 4.04 (m, 2H), 3.20 – 3.14 (m, 1H), 3.03 – 2.94 (m, 7H), 2.90 (s, 6H), 1.62 – 1.52 (m, 1H), 1.50 – 1.37 (m, 4H), 1.03 (t, 3H).
314	Ex. 127		*rac*-(6*R*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-2-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.50 – 8.46 (m, 1H), 8.28 – 8.20 (m, 2H), 7.71 – 7.67 (m, 1H), 7.41 – 7.36 (m, 2H), 7.23 – 7.16 (m, 2H), 6.92 (d, 1H), 5.07 – 4.92 (m, 2H), 4.41 – 4.28 (m, 2H), 4.17 – 4.04 (m, 3H), 3.10 – 3.03 (m, 1H), 3.02 – 2.94 (m, 6H), 2.90 (s, 6H), 1.39 (t, 3H), 1.18 (d, 3H), 1.00 (d, 3H).

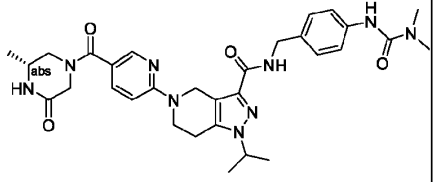
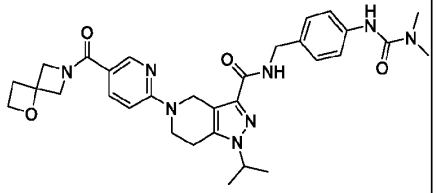
315	Ex. 567		(*S*)-*N*-(4-(3,3-bis(methyl-d_3)ureido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	552.6
316 ^	Ex. 127		*rel*-(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-2-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.67 – 8.62 (m, 1H), 8.29 – 8.25 (m, 2H), 7.72 – 7.69 (m, 1H), 7.48 – 7.43 (m, 2H), 7.28 – 7.20 (m, 2H), 6.81 (d, 1H), 5.13 – 4.96 (m, 2H), 4.45 – 4.40 (m, 2H), 4.37 – 4.30 (m, 1H), 4.29 – 4.19 (m, 2H), 3.10 – 3.04 (m, 1H), 2.98 (s, 6H), 2.93 – 2.89 (m, 6H), 1.32 – 1.23 (m, 6H), 0.92 – 0.87 (m, 3H).

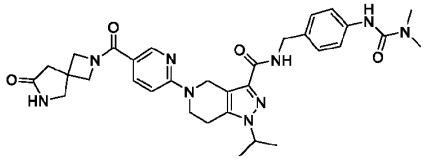
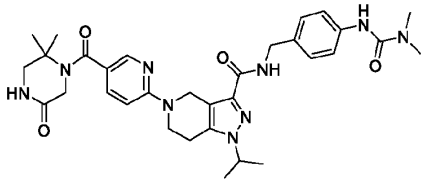
317 ^	Ex. 127		*rel*-(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-2-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.64 (t, 1H), 8.28 – 8.26 (m, 2H), 7.68 (dd, 1H), 7.49 – 7.44 (m, 2H), 7.27 – 7.22 (m, 2H), 6.77 (d, 1H), 5.10 – 4.97 (m, 2H), 4.42 (d, 2H), 4.38 – 4.30 (m, 1H), 4.29 – 4.17 (m, 2H), 3.11 – 3.03 (m, 1H), 2.98 (s, 6H), 2.94 – 2.88 (m, 6H), 1.31 – 1.22 (m, 6H), 0.89 (d, 3H).
318 ^	Ex. 77		(*S*)-1-((*R**)-*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.25 – 8.19 (m, 2H), 7.63 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.19 – 7.14 (m, 2H), 6.88 (d, 1H), 5.09 (d, 1H), 4.49 – 4.16 (m, 5H), 3.25 – 3.14 (m, 2H), 2.97 (s, 6H), 2.89 (s, 6H), 1.91 – 1.64 (m, 2H), 1.41 (d, 3H), 1.17 (d, 3H), 0.66 (t, 3H).

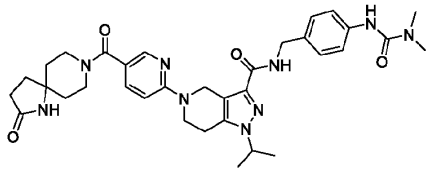
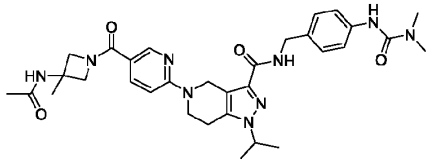
319 ^	Ex. 77		(*S*)-1-((*R**)-*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.25 – 8.20 (m, 2H), 7.63 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.20 – 7.13 (m, 2H), 6.88 (d, 1H), 5.10 (d, 1H), 4.50 – 4.17 (m, 5H), 3.25 – 3.14 (m, 2H), 2.97 (s, 6H), 2.89 (s, 6H), 2.05 - 1.70 (m, 2H), 1.35 (d, 3H), 1.23 – 1.16 (m, 3H), 0.77 (t, 3H).
320	Ex. 42[g]		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-(trifluoromethyl)cyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	599.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.54 (t, 1H), 8.30 (d, 1H), 7.71 (dd, 1H), 7.39 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 6.93 (d, 1H), 4.81 – 4.75 (m, 2H), 4.54 – 4.50 (m, 2H), 4.10 (t, 2H), 3.11 (s, 6H), 3.03 (s, 6H), 2.97 (t, 2H), 1.72 – 1.62 (m, 4H).

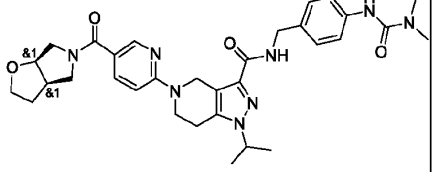
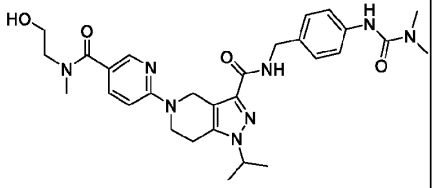
321	Ex. 113		*rac-(R)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(oxetan-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.28 (m, 1H), 7.63 (dd, 1H), 7.40 – 7.33 (m, 2H), 7.32 – 7.27 (m, 3H), 6.77 (d, 1H), 6.33 (s, 1H), 5.44 – 5.33 (m, 1H), 5.25 (t, 1H), 5.08 (t, 1H), 5.02 – 4.90 (m, 3H), 4.71 – 4.63 (m, 1H), 4.62 – 4.51 (m, 2H), 4.50 – 4.40 (m, 1H), 3.44 – 3.37 (m, 1H), 3.08 (s, 6H), 3.04 – 2.99 (m, 7H), 1.21 (d, 3H).
322	Ex. 322		*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	532.2; ^{1}H NMR (400 MHz, CD_3OD) δ 8.10 (d, 1H), 7.61 (dd, 1H), 7.39 – 7.35 (m, 2H), 7.34 – 7.28 (m, 2H), 6.91 (d, 1H), 4.81 – 4.76 (m, 1H), 4.70 (s, 2H), 4.56 – 4.50 (m, 3H), 4.12 – 3.87 (m, 4H), 3.05 – 3.03 (m, 6H), 2.87 (t, 2H), 2.36 – 2.24 (m, 1H), 2.15 – 2.00 (m, 2H), 1.90 – 1.77 (m, 1H), 1.49 (d, 6H).

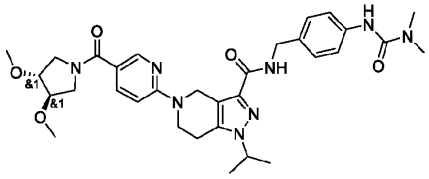
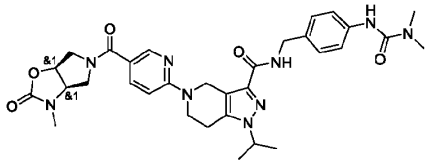
323	Ex. 126		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((6-(3,3-dimethylureido)pyridin-3-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	534.5
324	Ex. 125		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-((6-(3,3-dimethylureido)pyridin-3-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	535.4; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 9.66 (s, 1H), 8.72 – 8.66 (m, 1H), 8.51 (s, 2H), 8.24 – 8.21 (m, 1H), 8.00 – 7.89 (s, 1H), 7.69 (d, 1H), 5.40 (d, 1H), 4.68 (dd, 1H), 4.43 – 4.31 (m, 3H), 4.15 – 4.05 (m, 2H), 3.47 (dd, 1H), 3.28 – 3.22 (m, 1H), 3.18 – 2.95 (m, 12H), 1.39 (t, 3H), 1.16 (d, 3H).

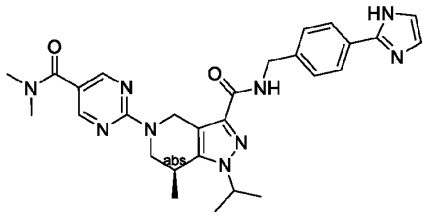
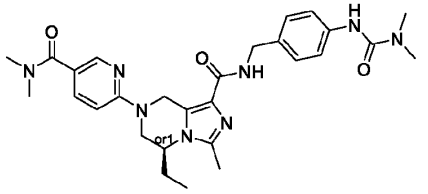
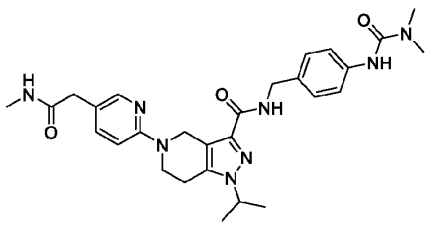
325	Ex. 193		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.5
326	Ex. 193		5-(5-(1-oxa-6-azaspiro[3.3]heptane-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.5

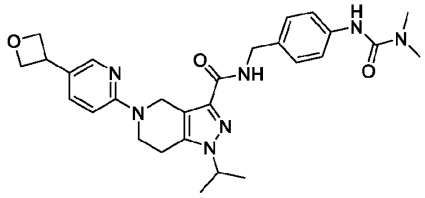
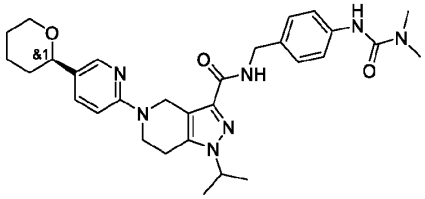
327	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(7-oxo-2,6-diazaspiro[3.4]octane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	614.5
328	Ex. 193		5-(5-(2,2-dimethyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.6

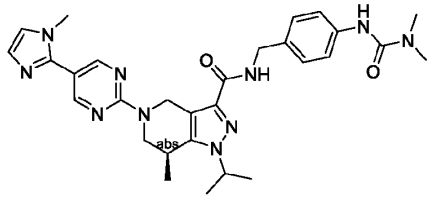
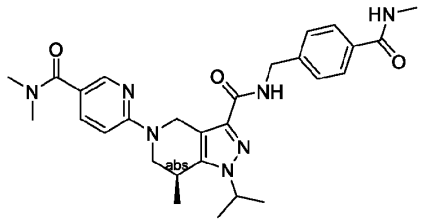
329	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxo-1,8-diazaspiro[4.5]decane-8-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.6
330	Ex. 193		5-(5-(3-acetamido-3-methylazetidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.5

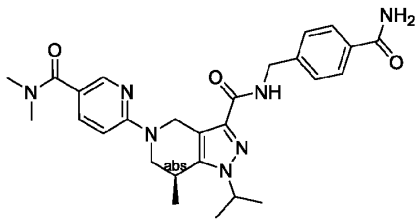
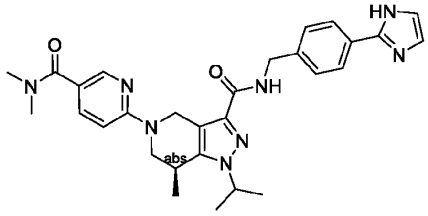
331	Ex. 193		*rac-N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((3*aR*,6*aR*)-hexahydro-2*H*-furo[2,3-*c*]pyrrole-5-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.5
332	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((2-hydroxyethyl)(methyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	563.5

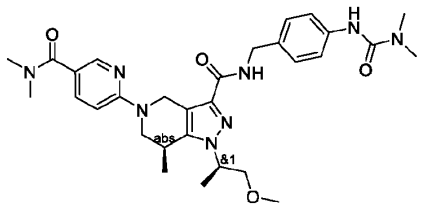
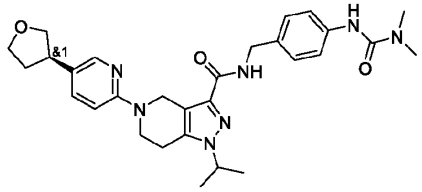
333	Ex. 193		*rac*-5-(5-((3*R*,4*R*)-3,4-dimethoxypyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	619.5
334	Ex. 193		*rac*-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-((3*aR*,6*aS*)-3-methyl-2-oxohexahydro-2*H*-pyrrolo[3,4-*d*]oxazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	630.6

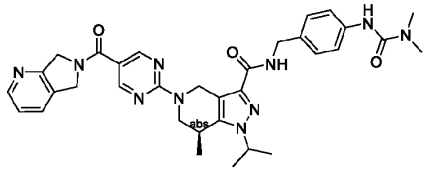
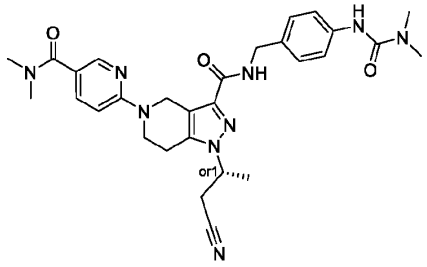
335 ^	Ex. 127		(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.42 (s, 1H), 8.51 – 8.45 (m, 3H), 7.86 – 7.82 (m, 2H), 7.37 – 7.32 (m, 2H), 7.19 (s, 1H), 6.96 (s, 1H), 5.44 (d, 1H), 4.75 – 4.69 (m, 1H), 4.55 – 4.23 (m, 4H), 3.42 – 3.36 (m, 2H), 2.96 (s, 6H), 1.44 – 1.36 (m, 6H), 1.12 (d, 3H).
336 ^	Ex. 23[g]		*rel-(R* or *S*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5-ethyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	533.3; 1H NMR (400 MHz, CD_3OD) δ 8.31 (d, 1H), 7.73 (dd, 1H), 7.35 – 7.30 (m, 2H), 7.28 – 7.23 (m, 2H), 6.88 (d, 1H), 5.27 – 5.10 (m, 2H), 4.68 – 4.60 (m, 2H), 4.48 (s, 2H), 4.35 – 4.28 (m, 1H), 3.09 (s, 6H), 2.99 (s, 6H), 2.39 (s, 3H), 1.76 – 1.65 (m, 2H), 1.06 (t, 3H).
337	Ex. 286		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methylamino)-2-oxoethyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.21 (s, 1H), 7.96 – 7.94 (m, 1H), 7.88 – 7.82 (m, 1H), 7.45 – 7.34 (m, 3H), 7.15 (d, 2H), 6.80 (d, 1H), 4.61 (s, 2H), 4.50 – 4.41 (m, 1H), 4.32 (d, 2H), 3.87 – 3.80 (m, 2H), 3.22 (s, 2H), 2.89 (s, 6H), 2.81 – 2.73 (m, 2H), 2.53 (d, 3H), 1.36 (d, 6H).

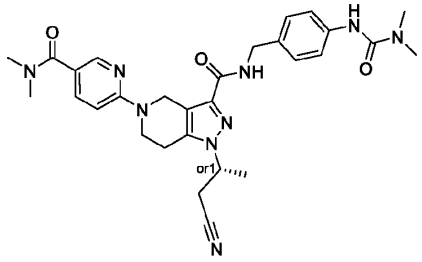
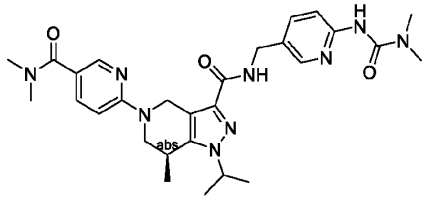
338	Ex. 338		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(oxetan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	518.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.06 (d, 1H), 7.79 (dd, 1H), 7.36 – 7.31 (m, 2H), 7.30 – 7.25 (m, 2H), 6.94 (d, 1H), 5.08 – 5.01 (m, 2H), 4.72 – 4.65 (m, 4H), 4.55 – 4.47 (m, 3H), 4.23 – 4.14 (m, 1H), 3.97 (t, 2H), 3.00 (s, 6H), 2.84 (t, 2H), 1.45 (d, 6H).
339	Ex. 322		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	546.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.08 (d, 1H), 7.59 (dd, 1H), 7.36 – 7.32 (m, 2H), 7.31 – 7.26 (m, 2H), 6.87 (d, 1H), 4.67 (s, 2H), 4.56 – 4.47 (m, 3H), 4.32 – 4.26 (m, 1H), 4.08 – 4.01 (m, 1H), 3.98 (t, 2H), 3.67 – 3.58 (m, 1H), 3.01 (s, 6H), 2.84 (t, 2H), 2.00 – 1.91 (m, 1H), 1.81 – 1.56 (m, 5H), 1.46 (d, 6H).

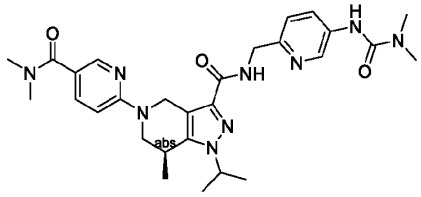
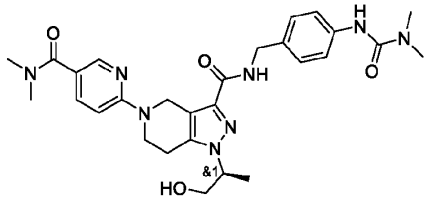
340	Ex. 127		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	557.6; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.50 (s, 2H), 8.32 (t, 1H), 8.21 (s, 1H), 7.68 (s, 1H), 7.39 – 7.34 (m, 2H), 7.18 – 7.12 (m, 2H), 7.01 (d, 1H), 5.41 (d, 1H), 4.75 – 4.68 (m, 1H), 4.55 – 4.46 (m, 1H), 4.39 – 4.25 (m, 3H), 3.61 (s, 3H), 3.27 – 3.20 (m, 2H), 2.88 (s, 6H), 1.43 – 1.35 (m, 6H), 1.15 (d, 3H).
341	Ex. 127		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	518.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.53 (t, 1H), 8.38 – 8.32 (m, 1H), 8.21 (d, 1H), 7.78 – 7.71 (m, 2H), 7.61 (dd, 1H), 7.38 – 7.31 (m, 2H), 6.86 (d, 1H), 5.07 (d, 1H), 4.58 – 4.33 (m, 4H), 4.27 – 4.12 (m, 1H), 3.28 – 3.16 (m, 2H), 2.95 (s, 6H), 2.75 (d, 3H), 1.44 – 1.34 (m, 6H), 1.18 (d, 3H).

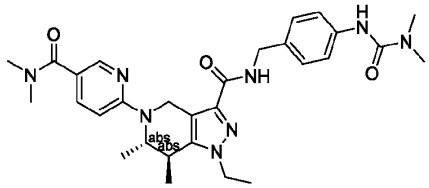
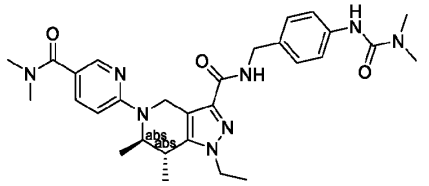
342	Ex. 127		(*S*)-*N*-(4-carbamoylbenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	504.1; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.55 (t, 1H), 8.24 (d, 1H), 7.94 – 7.88 (m, 1H), 7.85 – 7.79 (m, 2H), 7.64 (dd, 1H), 7.40 – 7.35 (m, 2H), 7.32 – 7.28 (m, 1H), 6.89 (d, 1H), 5.09 (d, 1H), 4.60 – 4.37 (m, 4H), 4.23 (d, 1H), 3.27 – 3.19 (m, 2H), 2.98 (s, 6H), 1.48 – 1.39 (m, 6H), 1.20 (d, 3H).
343	Ex. 127		(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	527.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.43 (s, 1H), 8.49 (t, 1H), 8.22 (d, 1H), 7.88 – 7.80 (m, 2H), 7.61 (dd, 1H), 7.38 – 7.31 (m, 2H), 7.20 (s, 1H), 6.97 (s, 1H), 6.87 (d, 1H), 5.08 (d, 1H), 4.59 – 4.35 (m, 4H), 4.22 (d, 1H), 3.25 – 3.16 (m, 2H), 2.95 (s, 6H), 1.48 – 1.33 (m, 6H), 1.18 (d, 3H).

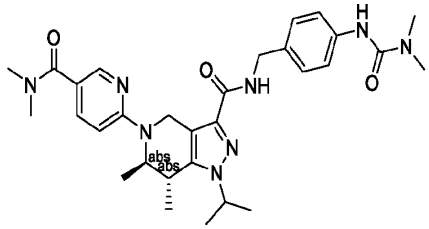
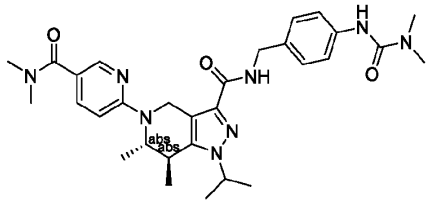
344	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-((*RS*)-1-methoxypropan-2-yl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	577.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.22 – 8.18 (m, 2H), 7.60 (dd, 1H), 7.39 – 7.32 (m, 2H), 7.17 – 7.11 (m, 2H), 6.85 (d, 1H), 5.15 – 5.01 (m, 1H), 4.53 – 4.12 (m, 5H), 3.76 – 3.49 (m, 2H), 3.25 – 3.15 (m, 2H), 3.13 (s, 3H), 2.94 (s, 6H), 2.87 (s, 6H), 1.37 – 1.27 (m, 3H), 1.21 – 1.13 (m, 3H).
345	Ex. 322		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	532.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.34 – 8.28 (m, 1H), 8.00 (d, 1H), 7.52 (dd, 1H), 7.34 – 7.30 (m, 2H), 7.28 – 7.24 (m, 2H), 6.86 (d, 1H), 4.64 – 4.62 (m, 2H), 4.53 – 4.45 (m, 3H), 4.07 – 4.00 (m, 2H), 3.96 – 3.84 (m, 3H), 3.63 – 3.57 (m, 1H), 3.37 – 3.32 (m, 1H), 2.99 (s, 6H), 2.82 (t, 2H), 2.37 – 2.27 (m, 1H), 2.00 – 1.87 (m, 1H), 1.44 (d, 6H).

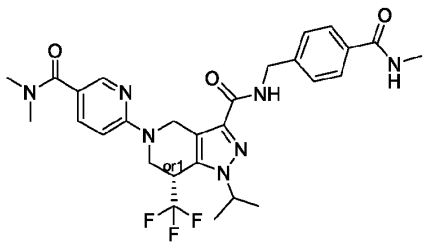
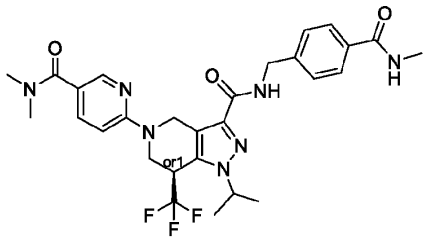
346	Ex. 127		(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	623.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.72 (d, 2H), 8.47 – 8.41 (m, 1H), 8.34 (t, 1H), 8.21 (s, 1H), 7.84 – 7.67 (m, 1H), 7.39 – 7.33 (m, 2H), 7.32 – 7.25 (m, 1H), 7.19 – 7.11 (m, 2H), 5.48 (d, 1H), 5.04 – 4.71 (m, 5H), 4.55 – 4.44 (m, 1H), 4.38 – 4.24 (m, 3H), 3.50 – 3.38 (m, 1H), 3.28 – 3.20 (m, 1H), 2.88 (s, 6H), 1.44 – 1.35 (m, 6H), 1.14 (d, 3H).
347 ^	Ex. 77[e]		*rel*-(*R* or *S*)-1-(1-cyanopropan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	558.1; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.37 (t, 1H), 8.27 – 8.22 (m, 2H), 7.66 (dd, 1H), 7.44 – 7.39 (m, 2H), 7.22 – 7.16 (m, 2H), 6.92 (d, 1H), 4.82 – 4.70 (m, 3H), 4.38 (d, 2H), 3.98 (t, 2H), 3.08 (d, 2H), 2.99 (s, 6H), 2.94 – 2.85 (m, 8H), 1.49 (d, 3H).

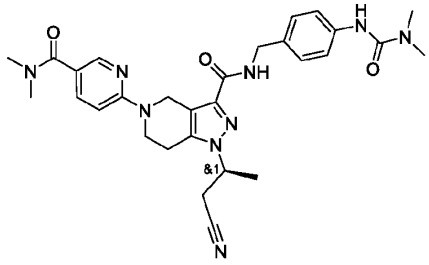
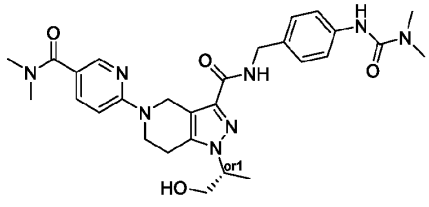
348 ^	Ex. 77[e]		*rel*-(*R* or *S*)-1-(1-cyanopropan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	558.1; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.37 (t, 1H), 8.27 – 8.21 (m, 2H), 7.66 (dd, 1H), 7.45 – 7.37 (m, 2H), 7.22 – 7.14 (m, 2H), 6.92 (d, 1H), 4.83 – 4.70 (m, 3H), 4.38 (d, 2H), 3.98 (t, 2H), 3.07 (d, 2H), 2.99 (s, 6H), 2.94 – 2.86 (m, 8H), 1.49 (d, 3H).
349	Ex. 127		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((6-(3,3-dimethylureido)pyridin-3-yl)methyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 9.88 – 9.70 (m, 1H), 8.63 – 8.57 (m, 1H), 8.27 – 8.20 (m, 2H), 8.06 – 7.99 (m, 1H), 7.71 – 7.62 (m, 2H), 6.94 – 6.88 (m, 1H), 5.09 (d, 1H), 4.59 – 4.50 (m, 1H), 4.45 – 4.33 (m, 3H), 4.25 – 4.19 (m, 1H), 3.37 – 3.32 (m, 1H), 3.28 – 3.21 (m, 1H), 3.00 – 2.94 (m, 12H), 1.45 – 1.40 (m, 6H), 1.21 – 1.18 (m, 3H).

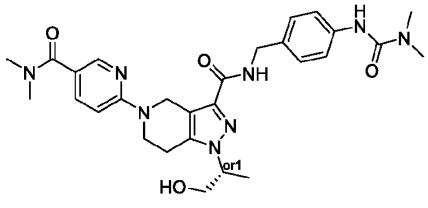
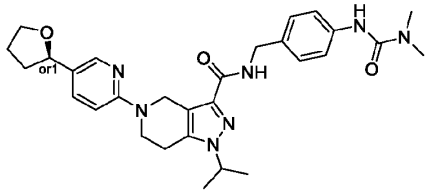
350	Ex. 127		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 8.96 – 8.86 (m, 1H), 8.85 – 8.76 (m, 1H), 8.67 – 8.59 (m, 1H), 8.25 – 8.17 (m, 2H), 7.69 – 7.55 (m, 2H), 6.95 – 6.88 (m, 1H), 5.09 (d, 1H), 4.66 – 4.50 (m, 3H), 4.43 – 4.40 (m, 1H), 4.22 (d, 1H), 3.37 – 3.34 (m, 1H), 3.29 – 3.24 (m, 1H), 3.00 – 2.97 (m, 6H), 2.96 – 2.93 (m, 6H), 1.47 – 1.42 (m, 6H), 1.22 – 1.19 (m, 3H).
351	Ex. 113^m		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-hydroxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	549.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.26 – 8.20 (m, 2H), 7.64 (dd, 1H), 7.43 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 6.89 (d, 1H), 4.90 – 4.69 (m, 3H), 4.39 – 4.21 (m, 3H), 4.00 – 3.86 (m, 2H), 3.66 – 3.56 (m, 2H), 2.98 (s, 6H), 2.91 (s, 6H), 2.86 – 2.80 (m, 2H), 1.37 (d, 3H).

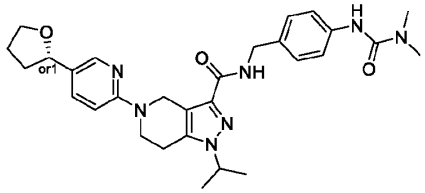
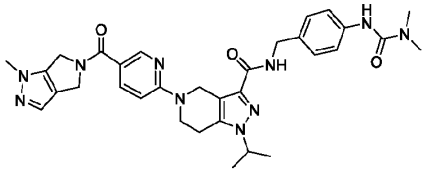
352 ^	Ex. 127		(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.27 (d, 1H), 8.22 (s, 1H), 7.66 (dd, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.16 (m, 2H), 6.86 (d, 1H), 5.09 – 4.92 (m, 2H), 4.40 – 4.26 (m, 2H), 4.15 – 4.04 (m, 3H), 3.09 – 3.02 (m, 1H), 3.01 – 2.94 (m, 6H), 2.90 (s, 6H), 1.38 (t, 3H), 1.18 (d, 3H), 0.99 (d, 3H).
353 ^	Ex. 127		(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.27 (d, 1H), 8.22 (s, 1H), 7.66 (dd, 1H), 7.40 – 7.36 (m, 2H), 7.20 – 7.16 (m, 2H), 6.86 (d, 1H), 5.07 – 4.92 (m, 2H), 4.40 – 4.27 (m, 2H), 4.16 – 4.04 (m, 3H), 3.08 – 3.02 (m, 1H), 3.01 – 2.94 (m, 6H), 2.90 (s, 6H), 1.38 (t, 3H), 1.18 (d, 3H), 0.99 (d, 3H).

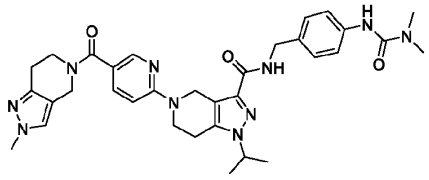
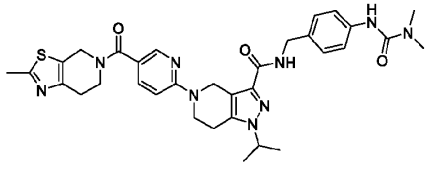
354 ^	Ex. 127		(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.36 (t, 1H), 8.27 (d, 1H), 8.23 (s, 1H), 7.66 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.21 – 7.17 (m, 2H), 6.86 (d, 1H), 5.05 – 4.94 (m, 2H), 4.58 – 4.48 (m, 1H), 4.40 – 4.28 (m, 2H), 4.10 (d, 1H), 3.09 – 3.02 (m, 1H), 3.01 – 2.93 (m, 6H), 2.91 (s, 6H), 1.45 (d, 3H), 1.40 (d, 3H), 1.17 (d, 3H), 0.99 (d, 3H).
355 ^	Ex. 127		(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.36 (t, 1H), 8.27 (d, 1H), 8.23 (s, 1H), 7.66 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.21 – 7.17 (m, 2H), 6.86 (d, 1H), 5.05 – 4.94 (m, 2H), 4.58 – 4.48 (m, 1H), 4.40 – 4.28 (m, 2H), 4.10 (d, 1H), 3.09 – 3.03 (m, 1H), 3.02 – 2.94 (m, 6H), 2.91 (s, 6H), 1.45 (d, 3H), 1.40 (d, 3H), 1.17 (d, 3H), 0.99 (d, 3H).

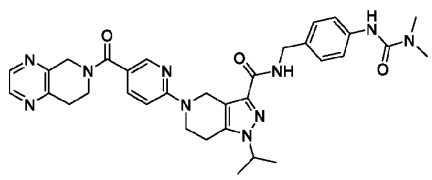
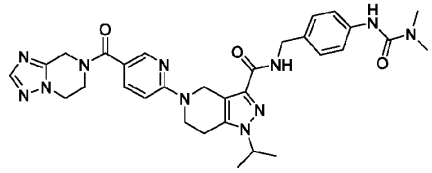
356 ^	Ex. 546		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	572.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.72 (t, 1H), 8.37 (q, 1H), 8.27 (d, 1H), 7.78 (d, 2H), 7.68 (dd, 1H), 7.40 (d, 2H), 6.83 (d, 1H), 5.27 (d, 1H), 5.06 (d, 1H), 4.72 – 4.64 (m, 1H), 4.56 – 4.43 (m, 3H), 4.27 (d, 1H), 3.31 – 3.27 (m, 1H), 2.98 (s, 6H), 2.77 (d, 3H), 1.44 (dd, 6H).
357 ^	Ex. 546		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	572.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.75 – 8.70 (m, 1H), 8.42 – 8.34 (m, 1H), 8.28 – 8.25 (m, 1H), 7.81 – 7.76 (m, 2H), 7.71 – 7.66 (m, 1H), 7.42 – 7.37 (m, 2H), 6.83 (d, 1H), 5.28 (d, 1H), 5.06 (d, 1H), 4.74 – 4.64 (m, 1H), 4.56 – 4.43 (m, 3H), 4.27 (d, 1H), 3.31 – 3.27 (m, 1H), 2.98 (s, 6H), 2.78 – 2.75 (m, 3H), 1.44 (dd, 6H).

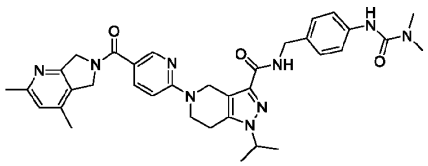
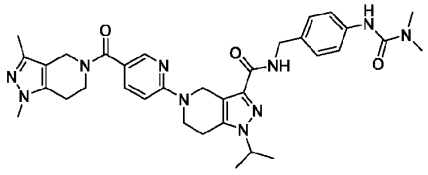
358	Ex. 77[e]		*rac*-(*R*)-1-(1-cyanopropan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	558.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.37 (t, 1H), 8.25 – 8.20 (m, 2H), 7.63 (dd, 1H), 7.41 – 7.35 (m, 2H), 7.20 – 7.13 (m, 2H), 6.89 (d, 1H), 4.80 – 4.68 (m, 3H), 4.35 (d, 2H), 3.95 (t, 2H), 3.06 (d, 2H), 2.96 (s, 6H), 2.91 – 2.82 (m, 8H), 1.46 (d, 3H).
359 ^	Ex. 353		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-hydroxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	549.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.34 (t, 1H), 8.21 – 8.19 (m, 2H), 7.60 (dd, 1H), 7.37 – 7.32 (m, 2H), 7.17 – 7.11 (m, 2H), 6.85 (d, 1H), 4.84 (t, 1H), 4.78 – 4.64 (m, 2H), 4.36 – 4.22 (m, 3H), 3.97 – 3.83 (m, 2H), 3.61 – 3.54 (m, 2H), 2.93 (s, 6H), 2.86 (s, 6H), 2.81 – 2.76 (m, 2H), 1.33 – 1.30 (m, 3H).

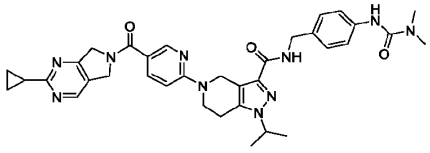
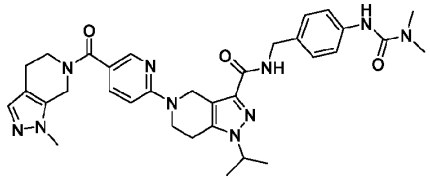
360 ^	Ex. 353		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-hydroxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	549.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.21 – 8.18 (m, 2H), 7.59 (dd, 1H), 7.38 – 7.32 (m, 2H), 7.16 – 7.11 (m, 2H), 6.84 (d, 1H), 4.83 (t, 1H), 4.78 – 4.64 (m, 2H), 4.37 – 4.22 (m, 3H), 3.97 – 3.82 (m, 2H), 3.61 – 3.53 (m, 2H), 2.93 (s, 6H), 2.86 (s, 6H), 2.81 – 2.75 (m, 2H), 1.37 – 1.32 – 1.29 (m, 3H).
361 ^	Ex. 322		*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	532.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s,1H), 7.53 – 7.43 (m, 1H), 7.38 – 7.23 (m, 4H), 7.17 – 7.10 (m, 1H), 6.84 – 6.75 (m, 1H), 6.31 (s, 1H), 4.81 – 4.64 (m, 3H), 4.60 – 4.50 (m, 2H), 4.42 – 4.30 (m, 1H), 4.14 – 3.99 (m, 3H), 3.93 - 3.83 (m, 1H), 3.03 (s, 6H), 2.83 – 2.73 (m, 2H), 2.30 – 2.17 (m, 1H), 2.08 – 1.95 (m, 2H), 1.85 – 1.73 (m, 1H), 1.49 – 1.38 (m, 6H).

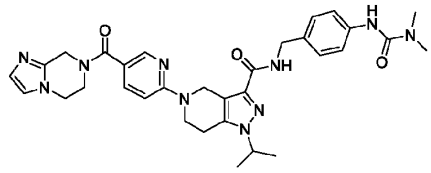
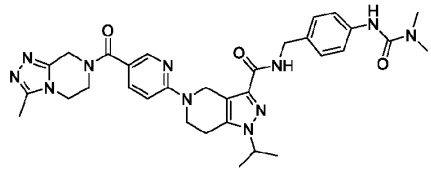
362 ^	Ex. 322		*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	532.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.09 (m, 1H), 7.52 – 7.44 (m, 1H), 7.38 – 7.24 (m, 4H), 7.18 – 7.10 (m, 1H), 6.84 – 6.75 (m, 1H), 6.33 – 6.26 (m, 1H), 4.81 – 4.65 (m, 3H), 4.60 – 4.50 (m, 2H), 4.42 – 4.31 (m, 1H), 4.14 – 3.97 (m, 3H), 3.93 – 3.82 (m, 1H), 3.03 (s, 6H), 2.83 – 2.73 (m, 2H), 2.30 – 2.19 (m, 1H), 2.07 – 1.94 (m, 2H), 1.86 – 1.75 (m, 1H), 1.44 (s, 6H).
363	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	611.8

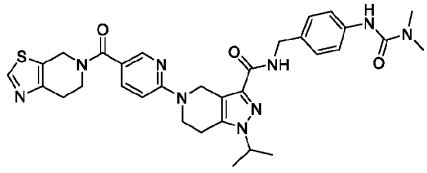
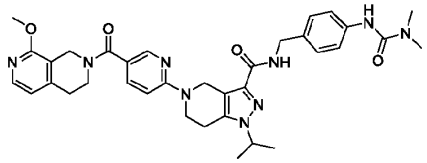
364	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.5
365	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydrothiazolo[5,4-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.7

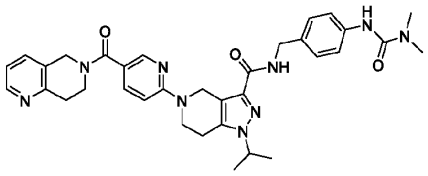
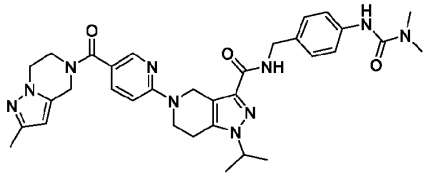
366	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydropyrido[3,4-*b*]pyrazine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	623.7
367	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.6

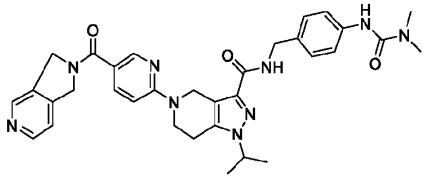
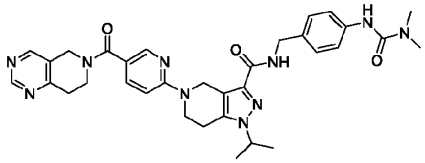
368	Ex. 193		5-(5-(2,4-dimethyl-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	636.7
369	Ex. 193		5-(5-(1,3-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	639.7

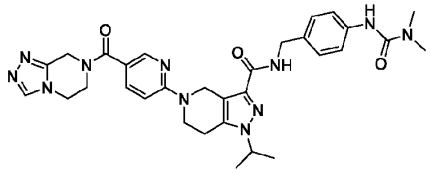
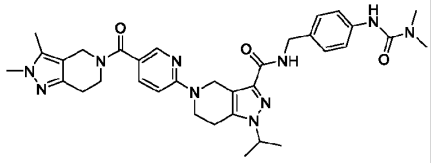
370	Ex. 193		5-(5-(2-cyclopropyl-6,7-dihydro-5*H*-pyrrolo[3,4-*d*]pyrimidine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	649.7
371	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.7

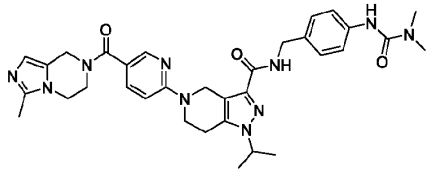
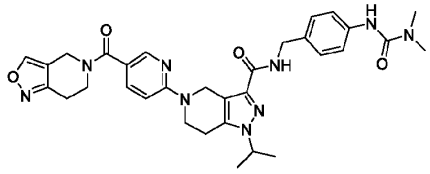
372	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	611.7
373	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	626.7

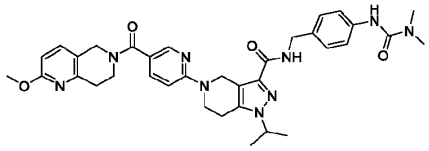
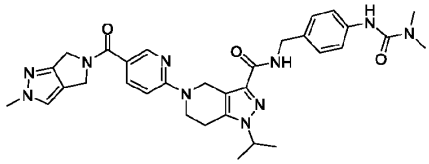
374	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydrothiazolo[5,4-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	628.6
375	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(8-methoxy-1,2,3,4-tetrahydro-2,7-naphthyridine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	652.8

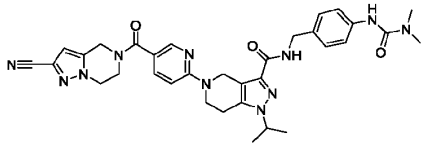
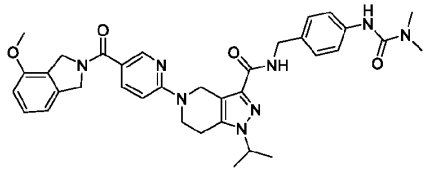
376	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-1,6-naphthyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	622.7
377	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.7

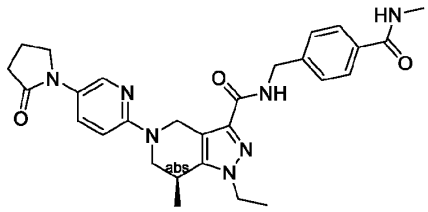
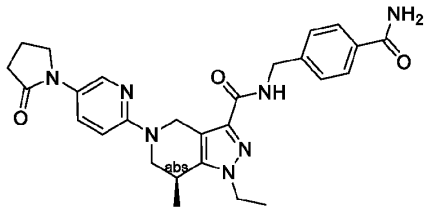
378	Ex. 193		5-(5-(2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	608.6
379	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydropyrido[4,3-*d*]pyrimidine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	623.7

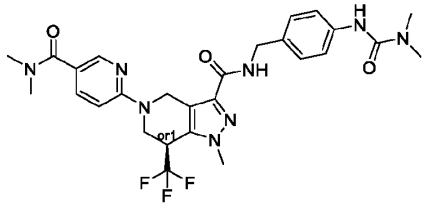
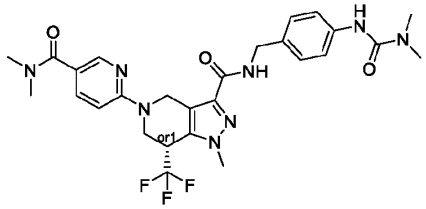
380	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.7
381	Ex. 193		5-(5-(2,3-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	639.6

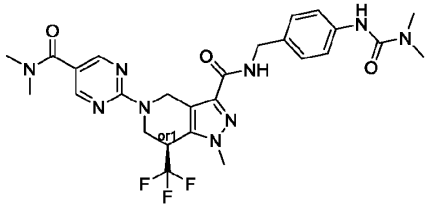
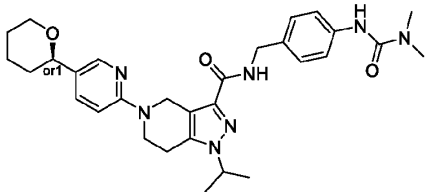
382	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.7
383	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydroisoxazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.5

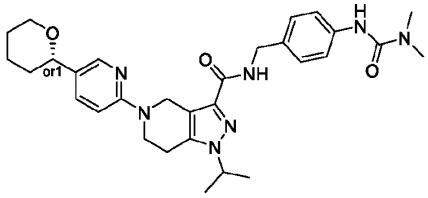
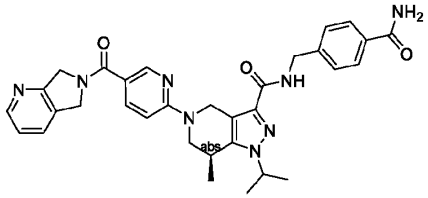
384	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methoxy-5,6,7,8-tetrahydro-1,6-naphthyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	652.7
385	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	611.7

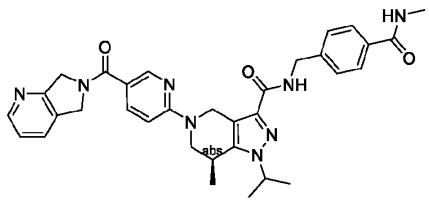
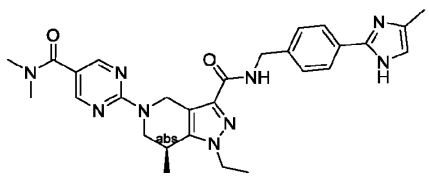
386	Ex. 193		5-(5-(2-cyano-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	636.7
387	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methoxyisoindoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	637.7

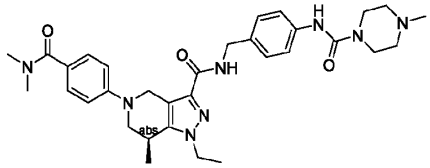
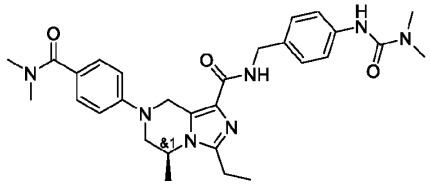
388	Ex. 77		(*S*)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	516.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.64 (t, 1H), 8.40 – 8.34 (m, 1H), 8.28 (d, 1H), 7.87 (dd, 1H), 7.79 – 7.72 (m, 2H), 7.40 – 7.33 (m, 2H), 6.89 (d, 1H), 4.89 (d, 1H), 4.49 – 4.37 (m, 2H), 4.28 – 4.06 (m, 4H), 3.79 – 3.73 (m, 2H), 3.23 – 3.15 (m, 1H), 2.77 (d, 3H), 2.47 – 2.40 (m, 3H), 2.12 – 2.00 (m, 2H), 1.39 (t, 3H), 1.21 (d, 3H).
389	Ex. 77		(*S*)-*N*-(4-carbamoylbenzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	502.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.64 (t, 1H), 8.28 (d, 1H), 7.93 – 7.85 (m, 2H), 7.84 – 7.80 (m, 2H), 7.39 – 7.28 (m, 3H), 6.89 (d, 1H), 4.90 (d, 1H), 4.49 – 4.41 (m, 2H), 4.30 – 4.07 (m, 4H), 3.80 – 3.74 (m, 2H), 3.24 – 3.16 (m, 1H), 2.47 – 2.39 (m, 3H), 2.12 – 1.99 (m, 2H), 1.40 (t, 3H), 1.22 (d, 3H).

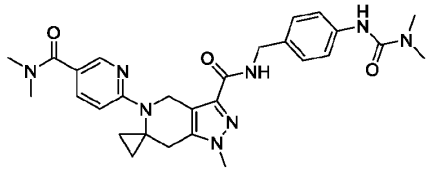
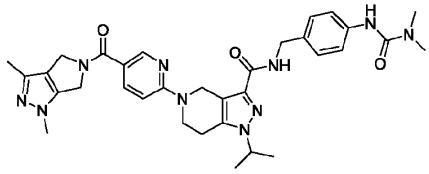
390	Ex. 39[f]		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.75 (t, 1H), 8.28 – 8.26 (m, 2H), 7.72 – 7.69 (m, 1H), 7.48 – 7.44 (m, 2H), 7.26 – 7.22 (m, 2H), 6.86 - 6.82 (m, 1H), 4.89 (d, 1H), 4.63 (dd, 1H), 4.51 (d, 1H), 4.43 (d, 2H), 4.05 – 3.98 (m, 1H), 3.96 (s, 3H), 3.82 (dd, 1H), 2.98 (s, 6H), 2.93 – 2.90 (m, 6H).
391 ^	Ex. 39[f]		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.75 (t, 1H), 8.27 (s, 2H), 7.71 (dd, 1H), 7.48 – 7.43 (m, 2H), 7.26 – 7.22 (m, 2H), 6.84 (d, 1H), 4.89 (d, 1H), 4.63 (dd, 1H), 4.51 (d, 1H), 4.43 (d, 2H), 4.05 – 3.98 (m, 1H), 3.96 (s, 3H), 3.82 (dd, 1H), 2.98 (s, 6H), 2.92 (s, 6H).

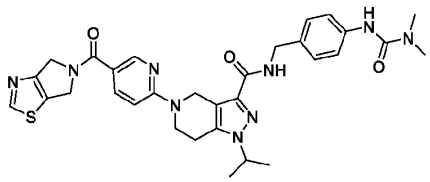
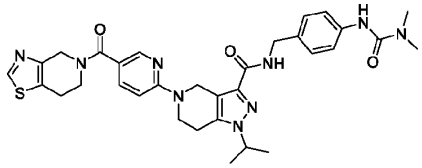
392 ^	Ex. 39[f]		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	574.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.83 (t, 1H), 8.56 (s, 2H), 8.26 (s, 1H), 7.47 – 7.42 (m, 2H), 7.25 – 7.20 (m, 2H), 5.27 (d, 1H), 4.90 (dd, 1H), 4.67 (d, 1H), 4.42 (d, 2H), 4.06 – 3.98 (m, 1H), 3.96 (s, 3H), 3.88 (dd, 1H), 3.06 – 2.94 (m, 6H), 2.92 (s, 6H).
393 ^	Ex. 322		*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	546.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.11 (m, 1H), 7.55 – 7.50 (m, 1H), 7.38 – 7.32 (m, 2H), 7.31 – 7.28 (m, 2H), 7.17 – 7.10 (m, 1H), 6.82 – 6.77 (m, 1H), 6.31 – 6.26 (m, 1H), 4.68 (s, 2H), 4.56 (d, 2H), 4.42 – 4.30 (m, 1H), 4.26 – 4.20 (m, 1H), 4.12 – 4.04 (m, 3H), 3.63 – 3.53 (m, 1H), 3.03 (s, 6H), 2.81 – 2.75 (m, 2H), 1.96 – 1.90 (m, 1H), 1.79 – 1.72 (m, 1H), 1.68 – 1.62 (m, 3H), 1.55 – 1.52 (m, 1H), 1.43 (d, 6H).

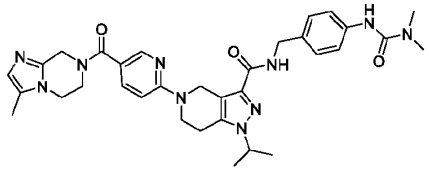
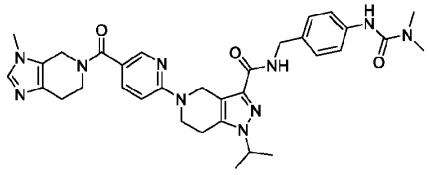
394 ^	Ex. 322		*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	546.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.11 (m, 1H), 7.54 – 7.50 (m, 1H), 7.38 – 7.33 (m, 2H), 7.31 - 7.28 (m, 2H), 7.16 – 7.11 (m, 1H), 6.79 (d, 1H), 6.29 (s, 1H), 4.68 (s, 2H), 4.56 (d, 2H), 4.40 – 4.31 (m, 1H), 4.25 – 4.20 (m, 1H), 4.12 – 4.04 (m, 3H), 3.63 – 3.54 (m, 1H), 3.03 (s, 6H), 2.78 (t, 2H), 1.96 – 1.89 (m, 1H), 1.79 – 1.73 (m, 1H), 1.68 – 1.61 (m, 3H), 1.55 – 1.52 (m, 1H), 1.43 (d, 6H).
395	Ex. 395		(*S*)-*N*-(4-carbamoylbenzyl)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	579.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.55 (t, 1H), 8.50 – 8.41 (m, 2H), 7.92 – 7.75 (m, 5H), 7.36 (d, 2H), 7.32 – 7.26 (m, 2H), 6.95 – 6.90 (m, 1H), 5.12 (d, 1H), 4.99 – 4.78 (m, 4H), 4.60 – 4.40 (m, 4H), 4.25 (d, 1H), 3.28 – 3.20 (m, 2H), 1.47 – 1.38 (m, 6H), 1.20 (d, 3H).

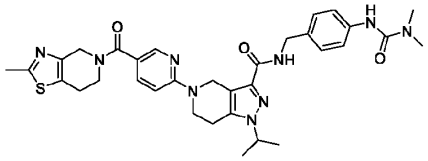
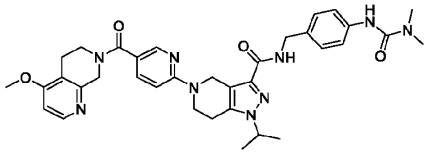
396	Ex. 395		(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	593.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.56 – 8.51 (m, 1H), 8.49 – 8.42 (m, 2H), 8.37 – 8.31 (m, 1H), 7.90 – 7.79 (m, 1H), 7.78 – 7.66 (m, 3H), 7.38 – 7.33 (m, 2H), 7.32 – 7.26 (m, 1H), 6.93 (d, 1H), 5.11 (d, 1H), 4.98 – 4.76 (m, 4H), 4.58 – 4.38 (m, 4H), 4.25 (d, 1H), 3.28 – 3.18 (m, 2H), 2.74 (d, 3H), 1.45 – 1.37 (m, 6H), 1.19 (d, 3H).
397	Ex. 127		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-7-methyl-*N*-(4-(4-methyl-1*H*-imidazol-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.21 – 12.09 (m, 1H), 8.60 (t, 1H), 8.51 (s, 2H), 7.84 – 7.77 (m, 2H), 7.33 (d, 2H), 6.92 – 6.63 (m, 1H), 5.42 (d, 1H), 4.67 (dd, 1H), 4.49 – 4.35 (m, 3H), 4.17 – 4.04 (m, 2H), 3.51 – 3.45 (m, 1H), 3.28 – 3.20 (m, 1H), 2.99 (s, 6H), 2.18 (d, 3H), 1.39 (t, 3H), 1.16 (d, 3H).

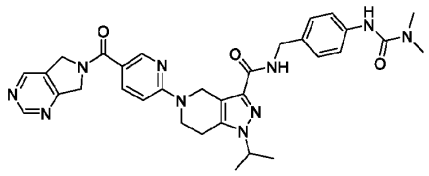
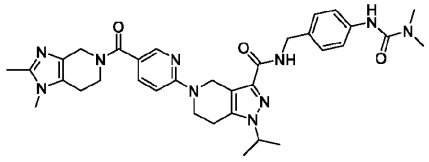
398	Ex. 537		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-ethyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.49 – 8.41 (m, 2H), 7.43 – 7.29 (m, 4H), 7.18 – 7.13 (m, 2H), 6.99 – 6.93 (m, 2H), 4.52 (d, 1H), 4.37 – 4.28 (m, 2H), 4.18 – 4.04 (m, 3H), 3.80 – 3.72 (m, 1H), 3.43 – 3.37 (m, 4H), 3.31 – 3.29 (m, 1H), 3.22 – 3.14 (m, 1H), 2.97 – 2.89 (m, 6H), 2.28 (t, 4H), 2.18 (s, 3H), 1.38 (t, 3H), 1.28 (d, 3H).
399	Ex. 537		*rac*-(*R*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	532.7; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.21 (s, 1H), 8.12 (t, 1H), 7.39 – 7.33 (m, 4H), 7.16 – 7.12 (m, 2H), 7.00 – 6.96 (m, 2H), 4.90 (d, 1H), 4.58 – 4.48 (m, 1H), 4.39 – 4.27 (m, 3H), 3.99 (d, 1H), 3.43 – 3.37 (m, 1H), 2.95 (s, 6H), 2.89 (s, 6H), 2.77 – 2.60 (m, 2H), 1.38 (d, 3H), 1.26 (t, 3H).

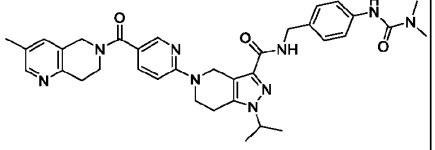
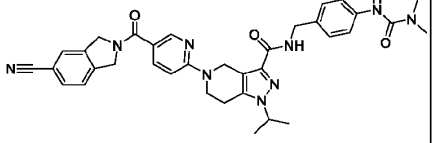
400	Ex. 23[l]		5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-methyl-1',4',5',7'-tetrahydrospiro[cyclopropane-1,6'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide	531.3; ^{1}H NMR (400 MHz, CD_3OD) δ 8.23 – 8.21 (m, 1H), 7.64 (dd, 1H), 7.34 – 7.29 (m, 2H), 7.27 – 7.23 (m, 2H), 7.18 – 7.14 (m, 1H), 5.99 – 5.90 (m, 1H), 4.52 – 4.39 (m, 2H), 4.26 – 4.16 (m, 1H), 3.70 (s, 3H), 3.53 – 3.34 (m, 1H), 3.05 (s, 6H), 2.99 (s, 6H), 2.25 – 2.15 (m, 1H), 1.36 – 1.25 (m, 2H), 0.93 – 0.80 (m, 2H).
401	Ex. 193		5-(5-(1,3-dimethyl-1,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrazole-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.6

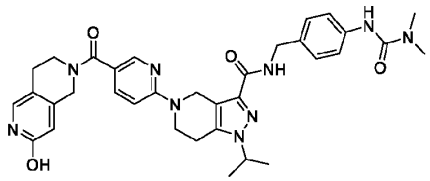
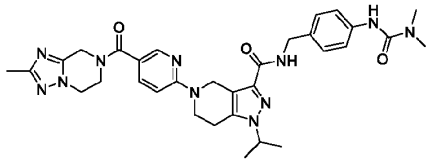
402	Ex. 193		5-(5-(5,6-dihydro-4*H*-pyrrolo[3,4-*d*]thiazole-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	614.8
403	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydrothiazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	628.8

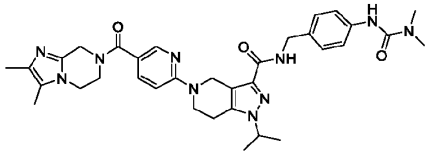
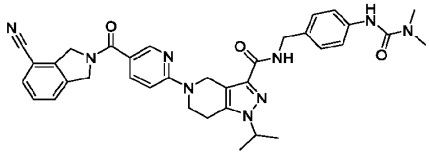
404	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.6
405	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-4,5,6,7-tetrahydro-3*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.7

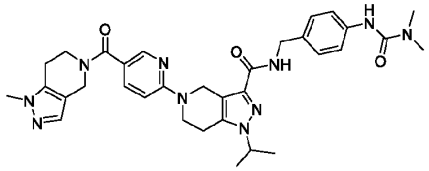
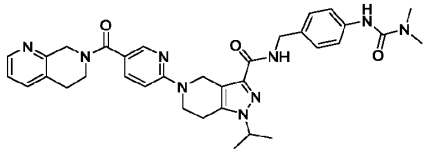
406	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydrothiazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.5
407	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methoxy-5,6,7,8-tetrahydro-1,7-naphthyridine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	652.6

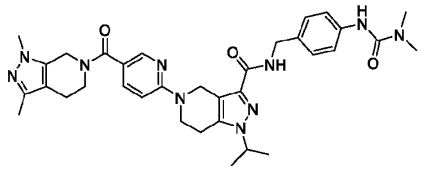
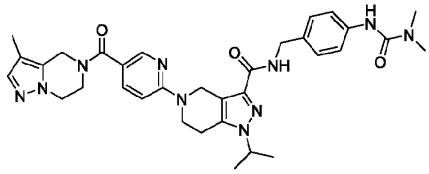
408	Ex. 193		5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*d*]pyrimidine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	609.5
409	Ex. 193		5-(5-(1,2-dimethyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	639.6

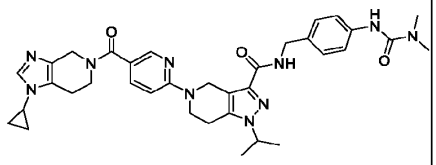
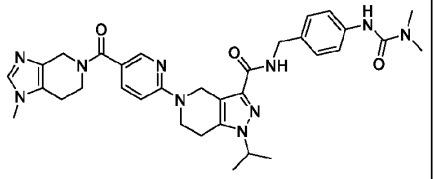
410	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydro-1,6-naphthyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	636.6
411	Ex. 193		5-(5-(5-cyanoisoindoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	632.8

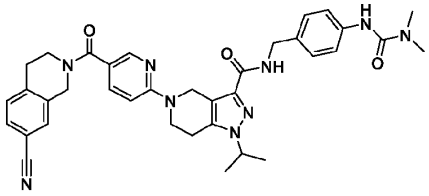
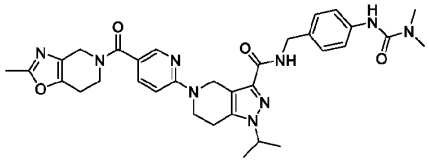
412	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(7-hydroxy-1,2,3,4-tetrahydro-2,6-naphthyridine-2-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	638.6
413	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	626.6

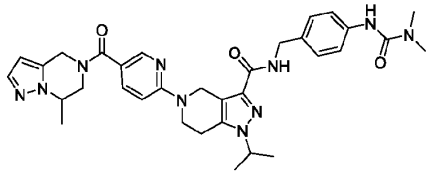
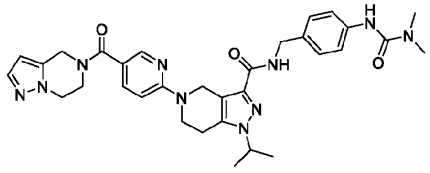
414	Ex. 193		5-(5-(2,3-dimethyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	639.8
415	Ex. 193		5-(5-(4-cyanoisoindoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	632.6

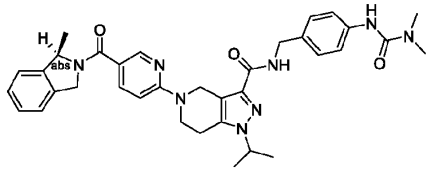
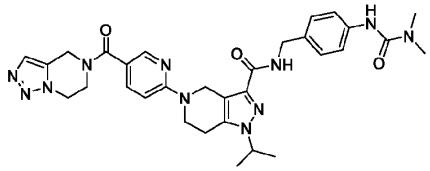
416	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.6
417	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-1,7-naphthyridine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	622.7

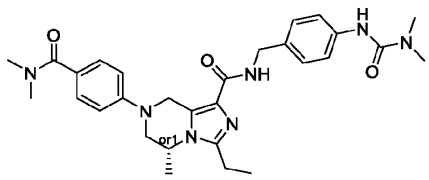
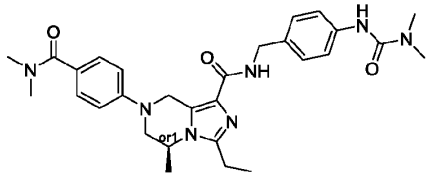
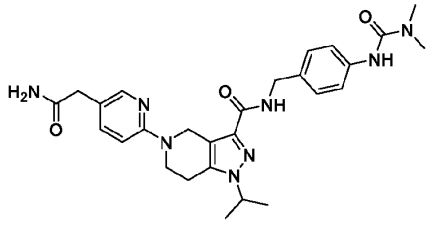
418	Ex. 193		5-(5-(1,3-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	639.6
419	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.5

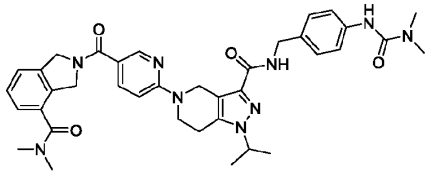
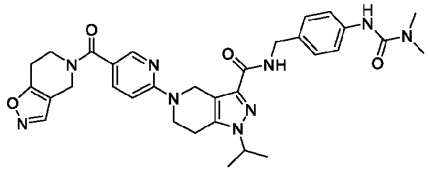
420	Ex. 193		5-(5-(1-cyclopropyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	651.8
421	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.7

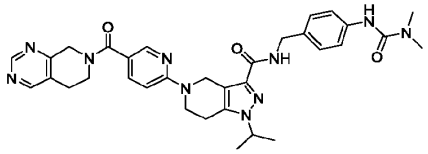
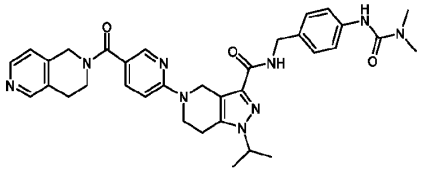
422	Ex. 193		5-(5-(7-cyano-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	646.8
423	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydrooxazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	626.6

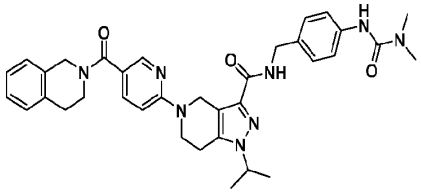
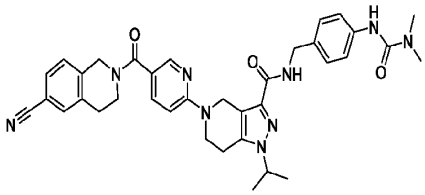
424	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(7-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	625.6
425	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	611.5

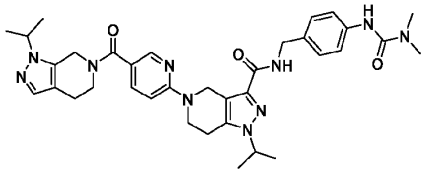
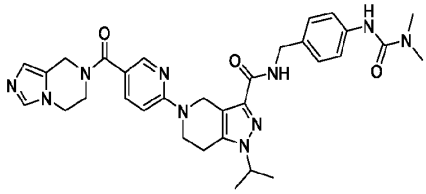
426	Ex. 193		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methylisoindoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	621.5
427	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.5

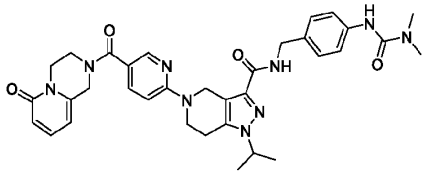
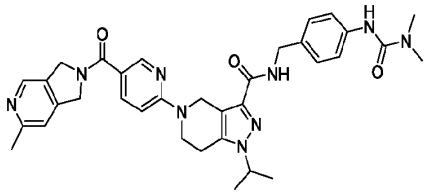
428 ^	Ex. 537		*rel*-(*R* or *S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	532.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.21 (s, 1H), 8.14 – 8.08 (m, 1H), 7.40 – 7.32 (m, 4H), 7.18 – 7.12 (m, 2H), 7.01 – 6.95 (m, 2H), 4.92 (d, 1H), 4.60 – 4.50 (m, 1H), 4.41 – 4.28 (m, 3H), 4.04 – 3.95 (m, 1H), 3.43 – 3.37 (m, 1H), 2.96 (s, 6H), 2.90 (s, 6H), 2.78 – 2.59 (m, 2H), 1.41 – 1.37 (m, 3H), 1.29 – 1.22 (m, 3H).
429 ^	Ex. 537		*rel*-(*R* or *S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	532.7; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.21 (s, 1H), 8.14 – 8.09 (m, 1H), 7.40 – 7.33 (m, 4H), 7.18 – 7.12 (m, 2H), 7.02 – 6.96 (m, 2H), 4.92 (d, 1H), 4.60 – 4.50 (m, 1H), 4.41 – 4.29 (m, 3H), 4.03 – 3.95 (m, 1H), 3.44 – 3.35 (m, 1H), 2.96 (s, 6H), 2.90 (s, 6H), 2.79 – 2.58 (m, 2H), 1.39 (d, 3H), 1.29 – 1.21 (m, 3H).
430	Ex. 286		5-(5-(2-amino-2-oxoethyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.32 – 8.23 (m, 1H), 8.20 (s, 1H), 7.95 (s, 1H), 7.46 – 7.30 (m, 4H), 7.20 – 7.10 (m, 2H), 6.86 – 6.74 (m, 2H), 4.60 (s, 2H), 4.50 – 4.39 (m, 1H), 4.35 – 4.28 (m, 2H), 3.88 – 3.74 (m, 2H), 3.23 – 3.16 (m, 2H), 2.88 (s, 6H), 2.79 – 2.72 (m, 2H), 1.36 (d, 6H).

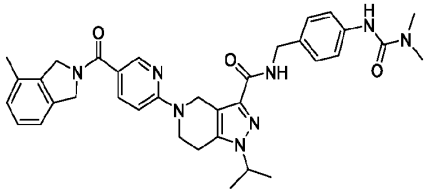
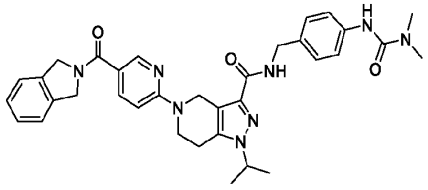
431	Ex. 193		5-(5-(4-(dimethylcarbamoyl)isoindoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	678.8
432	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydroisoxazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.8

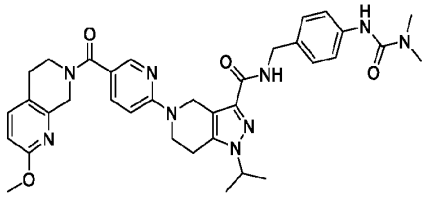
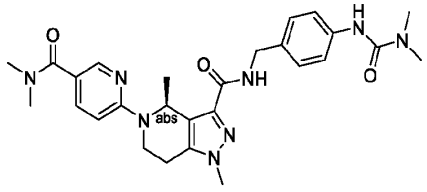
433	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydropyrido[3,4-*d*]pyrimidine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	623.6
434	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1,2,3,4-tetrahydro-2,6-naphthyridine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	622.6

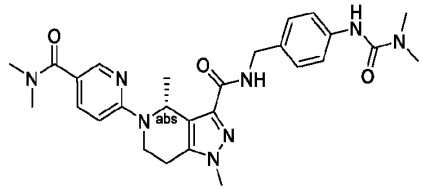
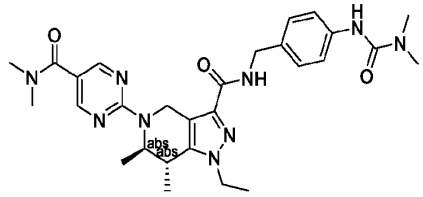
435	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1,2,3,4-tetrahydroisoquinoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	621.8
436	Ex. 193		5-(5-(6-cyano-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	646.8

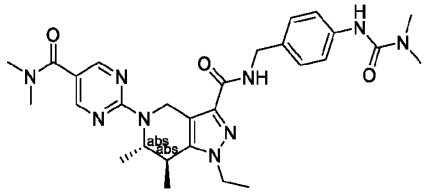
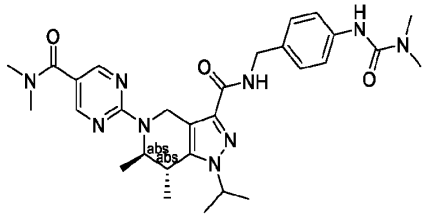
437	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	653.8
438	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	611.7

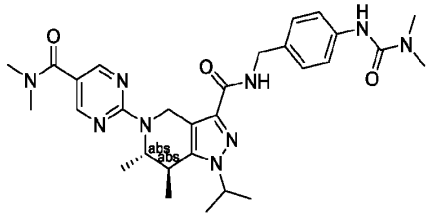
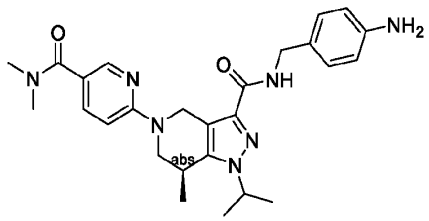
439	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-1,3,4,6-tetrahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	638.8
440	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-methyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	622.6

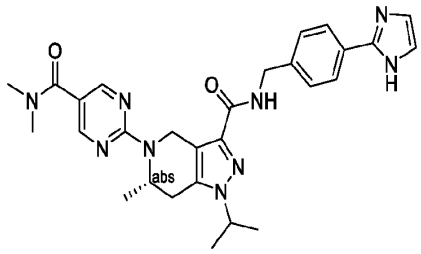
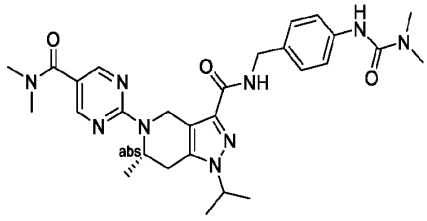
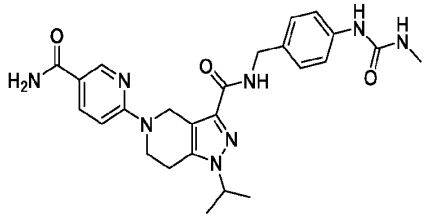
441	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methylisoindoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	621.8
442	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(isoindoline-2-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	607.8

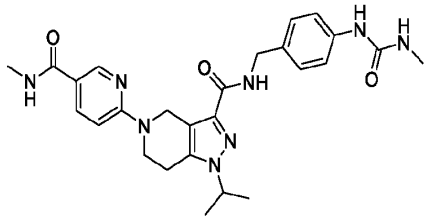
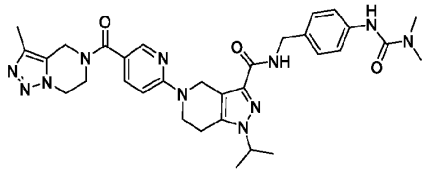
443	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methoxy-5,6,7,8-tetrahydro-1,7-naphthyridine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	652.7
444 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,4-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.42 – 8.36 (m, 1H), 8.20 – 8.13 (m, 2H), 7.60 – 7.51 (m, 1H), 7.36 – 7.27 (m, 2H), 7.14 – 7.05 (m, 2H), 6.84 – 6.76 (m, 1H), 5.82 – 5.71 (m, 1H), 4.60 – 4.48 (m, 1H), 4.38 – 4.18 (m, 2H), 3.73 – 3.64 (m, 3H), 3.40 – 3.38 (m, 1H), 2.95 – 2.88 (m, 6H), 2.87 – 2.81 (m, 6H), 2.73 – 2.65 (m, 2H), 1.41 – 1.34 (m, 3H).

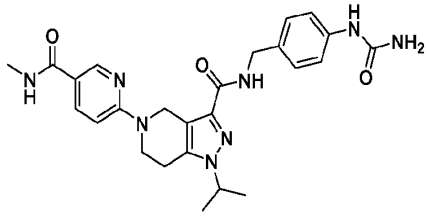
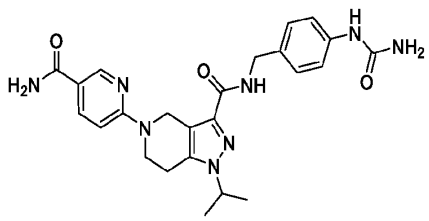
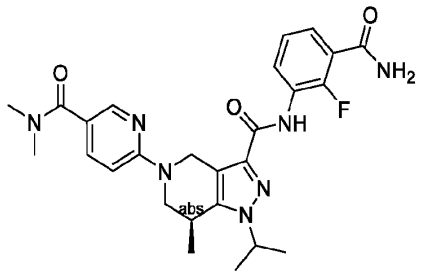
445 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,4-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.45 – 8.41 (m, 1H), 8.23 – 8.20 (m, 2H), 7.61 (dd, 1H), 7.39 – 7.35 (m, 2H), 7.17 – 7.12 (m, 2H), 6.88 – 6.83 (m, 1H), 5.84 – 5.76 (m, 1H), 4.64 – 4.53 (m, 1H), 4.42 – 4.22 (m, 2H), 3.73 (s, 3H), 3.43 – 3.36 (m, 1H), 2.96 (s, 6H), 2.90 (s, 6H), 2.78 – 2.69 (m, 2H), 1.43 (d, 3H).
446 ^	Ex. 23[k]		(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-*1H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.57 – 8.50 (m, 2H), 8.49 – 8.42 (m, 1H), 8.25 – 8.20 (m, 1H), 7.42 – 7.35 (m, 2H), 7.21 – 7.14 (m, 2H), 5.52 – 5.45 (m, 1H), 5.35 – 5.26 (m, 1H), 4.41 – 4.25 (m, 2H), 4.19 – 4.06 (m, 3H), 3.10 – 3.04 (m, 1H), 3.03 – 2.95 (m, 6H), 2.94 – 2.88 (m, 6H), 1.44 – 1.33 (m, 3H), 1.17 – 1.11 (m, 3H), 1.09 – 1.01 (m, 3H).

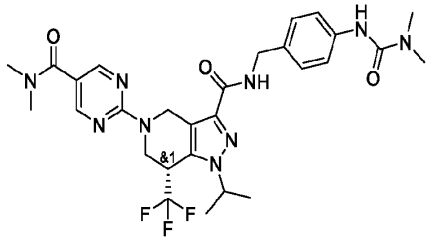
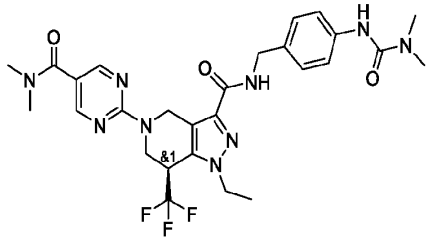
447 ^	Ex. 23[k]		(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-*1H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.53 (s, 2H), 8.46 (t, 1H), 8.22 (s, 1H), 7.40 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 5.51 – 5.45 (m, 1H), 5.30 (q, 1H), 4.38 – 4.27 (m, 2H), 4.17 – 4.06 (m, 3H), 3.10 – 3.05 (m, 1H), 3.04 – 2.94 (m, 6H), 2.91 – 2.89 (m, 6H), 1.40 – 1.35 (m, 3H), 1.15 – 1.11 (m, 3H), 1.08 – 1.04 (m, 3H).
448 ^	Ex. 4[k]		(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	562.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.53 (s, 2H), 8.36 (t, 1H), 8.23 (s, 1H), 7.41 – 7.37 (m, 2H), 7.21 – 7.17 (m, 2H), 5.47 (d, 1H), 5.33 – 5.27 (m, 1H), 4.55 – 4.46 (m, 1H), 4.40 – 4.28 (m, 2H), 4.15 (d, 1H), 3.12 – 3.05 (m, 1H), 3.04 – 2.94 (m, 6H), 2.91 (s, 6H), 1.45 (d, 3H), 1.40 (d, 3H), 1.13 (d, 3H), 1.06 (d, 3H).

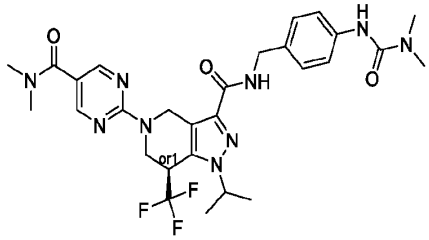
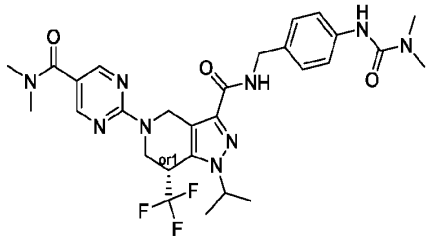
449 ^	Ex. 4[k]		(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	562.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.57 – 8.50 (m, 2H), 8.36 (t, 1H), 8.23 (s, 1H), 7.43 – 7.37 (m, 2H), 7.21 – 7.17 (m, 2H), 5.47 (d, 1H), 5.34 – 5.27 (m, 1H), 4.55 – 4.46 (m, 1H), 4.40 – 4.28 (m, 2H), 4.15 (d, 1H), 3.12 – 3.05 (m, 1H), 3.04 – 2.94 (m, 6H), 2.91 (s, 6H), 1.45 (d, 3H), 1.40 (d, 3H), 1.13 (d, 3H), 1.06 (d, 3H).
450	Ex. 128		(*S*)-*N*-(4-aminobenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	476.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.25 – 8.22 (m, 1H), 8.12 (t, 1H), 7.65 – 7.60 (m, 1H), 7.01 – 6.96 (m, 2H), 6.88 (d, 1H), 6.52 – 6.47 (m, 2H), 5.08 (d, 1H), 4.93 (s, 2H), 4.59 – 4.46 (m, 1H), 4.43 – 4.35 (m, 1H), 4.29 – 4.16 (m, 3H), 3.25 – 3.15 (m, 2H), 2.97 (s, 6H), 1.44 – 1.35 (m, 6H), 1.21 – 1.15 (m, 3H).

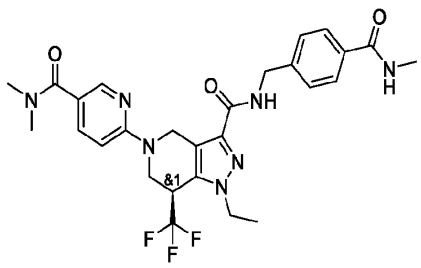
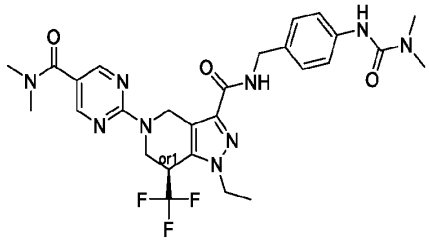
451	Ex. 125[e]		(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.5; ^{1}H NMR* (600 MHz, $(CD_3)_2SO$) δ 14.58 (s, 1H), 8.63 (t, 1H), 8.53 – 8.52 (m, 2H), 7.97 – 7.92 (m, 2H), 7.80 (s, 2H), 7.60 – 7.55 (m, 2H), 5.63 – 5.55 (m, 2H), 4.56 – 4.46 (m, 3H), 4.14 (d, 1H), 3.04 – 2.92 (m, 7H), 2.82 – 2.77 (m, 1H), 1.45 (d, 3H), 1.39 (d, 3H), 1.16 – 1.12 (m, 3H).
452	Ex. 125[e]		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.5; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.54 – 8.52 (m, 2H), 8.34 (t, 1H), 8.23 (s, 1H), 7.42 – 7.37 (m, 2H), 7.21 – 7.15 (m, 2H), 5.65 – 5.53 (m, 2H), 4.55 – 4.46 (m, 1H), 4.34 (d, 2H), 4.15 (d, 1H), 3.03 – 2.94 (m, 6H), 2.93 – 2.87 (m, 7H), 2.81 – 2.74 (m, 1H), 1.43 (d, 3H), 1.37 (d, 3H), 1.14 (d, 3H).
453	Ex. 193		5-(5-carbamoylpyridin-2-yl)-1-isopropyl-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	491.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.63 (d, 1H), 8.43 (s, 1H), 8.32 (t, 1H), 7.98 (dd, 1H), 7.80 – 7.72 (m, 1H), 7.35 – 7.29 (m, 2H), 7.20 – 7.09 (m, 3H), 6.88 (d, 1H), 5.94 (q, 1H), 4.76 (s, 2H), 4.53 – 4.43 (m, 1H), 4.33 (d, 2H), 3.96 (t, 2H), 2.81 (t, 2H), 2.62 (d, 3H), 1.38 (d, 6H).

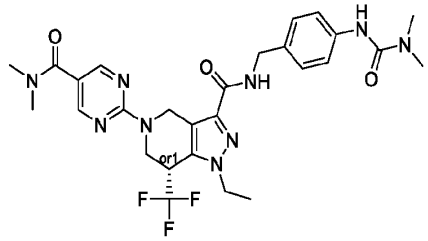
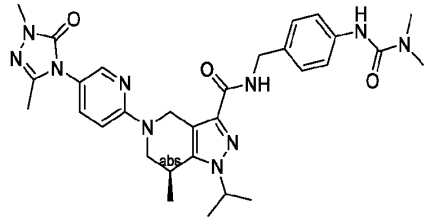
454	Ex. 193		1-isopropyl-5-(5-(methylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	505.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.58 (d, 1H), 8.43 (s, 1H), 8.32 (t, 1H), 8.21 (q, 1H), 7.94 (dd, 1H), 7.34 – 7.27 (m, 2H), 7.20 – 7.13 (m, 2H), 6.88 (d, 1H), 5.94 (q, 1H), 4.74 (s, 2H), 4.53 – 4.40 (m, 1H), 4.32 (d, 2H), 3.95 (t, 2H), 2.80 (t, 2H), 2.74 (d, 3H), 2.61 (d, 3H), 1.38 (d, 6H).
455	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	626.7

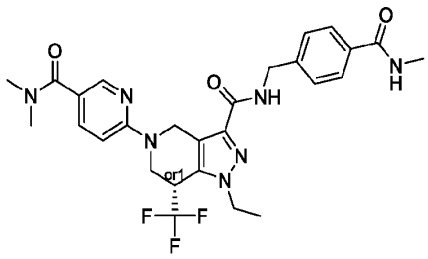
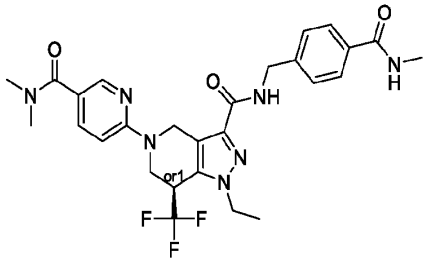
456	Ex. 193		1-isopropyl-5-(5-(methylcarbamoyl)pyridin-2-yl)-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	491.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.58 (d, 1H), 8.45 (s, 1H), 8.32 (t, 1H), 8.21 (q, 1H), 7.94 (dd, 1H), 7.34 – 7.27 (m, 2H), 7.19 – 7.14 (m, 2H), 6.88 (d, 1H), 5.78 (s, 2H), 4.74 (s, 2H), 4.51 – 4.41 (m, 1H), 4.32 (d, 2H), 3.95 (t, 2H), 2.80 (t, 2H), 2.73 (d, 3H), 1.40 – 1.32 (m, 6H).
457	Ex. 193		5-(5-carbamoylpyridin-2-yl)-1-isopropyl-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	477.1; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (d, 1H), 8.46 (s, 1H), 8.31 (t, 1H), 7.97 (dd, 1H), 7.79 – 7.72 (m, 1H), 7.34 – 7.28 (m, 2H), 7.19 – 7.09 (m, 3H), 6.88 (d, 1H), 5.78 (s, 2H), 4.75 (s, 2H), 4.54 – 4.41 (m, 1H), 4.32 (d, 2H), 3.96 (t, 2H), 2.80 (t, 2H), 1.38 (d, 6H).
458	Ex. 127		(*S*)-*N*-(3-carbamoyl-2-fluorophenyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	508.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.42 (s, 1H), 8.24 (d, 1H), 8.08 – 8.02 (m, 1H), 7.78 (s, 1H), 7.68 – 7.60 (m, 2H), 7.45 – 7.38 (m, 1H), 7.26 (t, 1H), 6.92 (d, 1H), 5.15 (d, 1H), 4.66 – 4.54 (m, 1H), 4.47 – 4.39 (m, 1H), 4.28 (d, 1H), 3.41 – 3.36 (m, 2H), 2.97 (s, 6H), 1.50 – 1.42 (m, 6H), 1.22 (d, 3H).

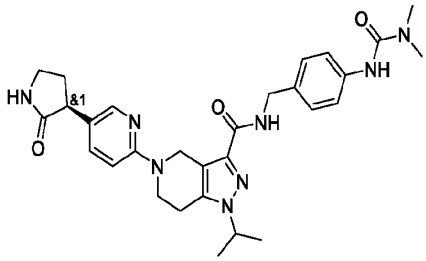
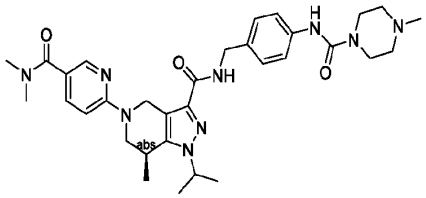
459	Ex. 530		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 – 8.44 (m, 3H), 8.17 (s, 1H), 7.36 – 7.30 (m, 2H), 7.16 – 7.08 (m, 2H), 5.51 – 5.39 (m, 2H), 4.65 – 4.54 (m, 1H), 4.50 – 4.41 (m, 1H), 4.36 – 4.19 (m, 3H), 3.26 – 3.24 (m, 1H), 2.93 (s, 6H), 2.84 (s, 6H), 1.36 (dd, 6H).
460	Ex. 530		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	588.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 2H), 7.37 – 7.33 (m, 2H), 7.31 – 7.28 (m, 2H), 7.10 (t, 1H), 6.31 (s, 1H), 5.87 – 5.67 (m, 2H), 4.64 – 4.42 (m, 3H), 4.12 (q, 2H), 3.68 – 3.56 (m, 1H), 3.35 – 3.25 (m, 1H), 3.10 (s, 6H), 3.03 (s, 6H), 1.47 (t, 3H).

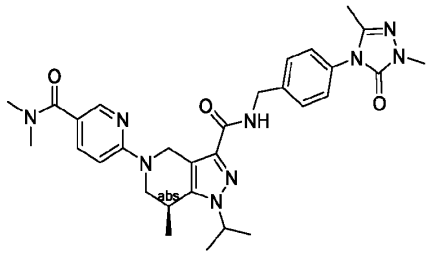
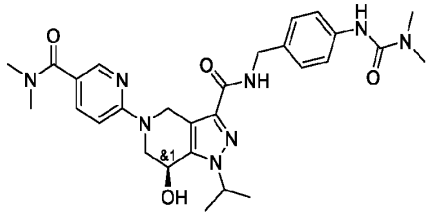
461 ^	Ex. 530		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.56 – 8.48 (m, 3H), 8.22 (s, 1H), 7.40 – 7.34 (m, 2H), 7.19 – 7.13 (m, 2H), 5.56 – 5.43 (m, 2H), 4.70 – 4.59 (m, 1H), 4.57 – 4.47 (m, 1H), 4.40 – 4.25 (m, 3H), 3.45 – 3.37 (m, 1H), 2.98 (s, 6H), 2.88 (s, 6H), 1.41 (dd, 6H).
462 ^	Ex. 530		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.57 – 8.48 (m, 3H), 8.22 (s, 1H), 7.41 – 7.34 (m, 2H), 7.20 – 7.13 (m, 2H), 5.57 – 5.42 (m, 2H), 4.69 – 4.59 (m, 1H), 4.56 – 4.47 (m, 1H), 4.39 – 4.25 (m, 3H), 3.43 – 3.39 (m, 1H), 2.98 (s, 6H), 2.89 (s, 6H), 1.41 (dd, 6H).

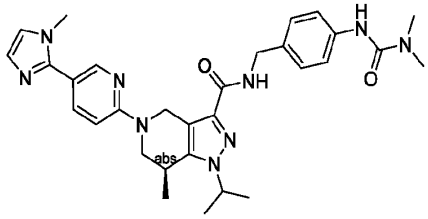
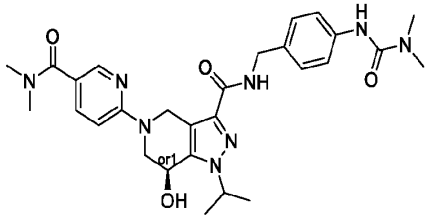
463	Ex. 39[l]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	558.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.84 – 8.78 (m, 1H), 8.40 – 8.34 (m, 1H), 8.27 (d, 1H), 7.80 – 7.76 (m, 2H), 7.68 (dd, 1H), 7.41 – 7.36 (m, 2H), 6.84 (d, 1H), 5.32 – 5.03 (m, 2H), 4.54 – 4.44 (m, 3H), 4.31 – 4.15 (m, 3H), 3.29 – 3.23 (m, 1H), 2.98 (s, 6H), 2.77 (d, 3H), 1.43 (t, 3H).
464 ^	Ex. 530		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	588.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.64 – 8.59 (m, 1H), 8.57 (s, 2H), 8.23 (s, 1H), 7.43 – 7.37 (m, 2H), 7.21 – 7.16 (m, 2H), 5.61 – 5.45 (m, 2H), 4.55 – 4.45 (m, 1H), 4.41 – 4.28 (m, 3H), 4.22 – 4.14 (m, 2H), 3.43 – 3.38 (m, 1H), 3.00 (s, 6H), 2.91 (s, 6H), 1.42 (t, 3H).

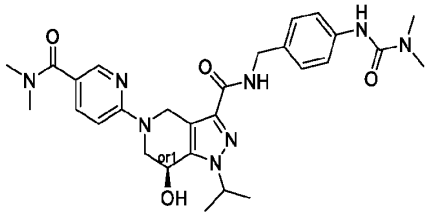
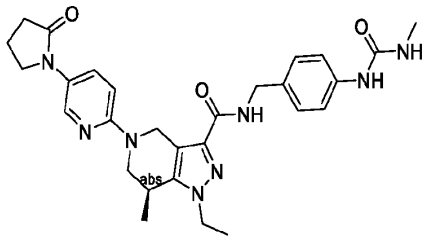
465 ^	Ex. 530		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	588.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.64 – 8.59 (m, 1H), 8.57 (s, 2H), 8.23 (s, 1H), 7.43 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 5.62 – 5.44 (m, 2H), 4.54 – 4.44 (m, 1H), 4.41 – 4.28 (m, 3H), 4.23 – 4.14 (m, 2H), 3.44 – 3.37 (m, 1H), 3.00 (s, 6H), 2.91 (s, 6H), 1.42 (t, 3H).
466	Ex. 127		(*S*)-5-(5-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.35 (t, 1H), 8.23 (s, 1H), 8.12 (d, 1H), 7.59 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.21 – 7.15 (m, 2H), 7.00 (d, 1H), 5.06 (d, 1H), 4.60 – 4.49 (m, 1H), 4.45 – 4.21 (m, 4H), 3.39 – 3.35 (m, 1H), 3.32 – 3.31 (m, 3H), 3.28 – 3.19 (m, 1H), 2.90 (s, 6H), 2.04 (s, 3H), 1.43 (dd, 6H), 1.22 (d, 3H).

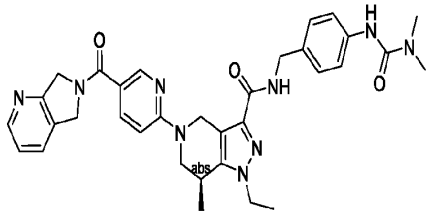
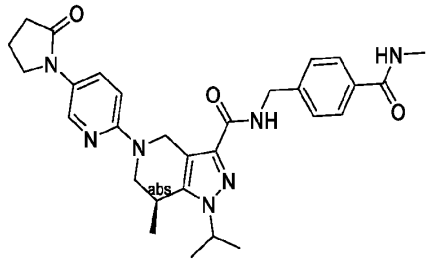
467 ^	Ex. 39		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	558.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.81 (t, 1H), 8.40 – 8.34 (m, 1H), 8.27 (d, 1H), 7.80 – 7.74 (m, 2H), 7.68 (dd, 1H), 7.41 – 7.35 (m, 2H), 6.83 (d, 1H), 5.31 – 5.00 (m, 2H), 4.54 – 4.41 (m, 3H), 4.32 – 4.14 (m, 3H), 3.30 – 3.24 (m, 1H), 2.98 (s, 6H), 2.76 (d, 3H), 1.42 (t, 3H).
468 ^	Ex. 39		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	558.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.81 (t, 1H), 8.40 – 8.34 (m, 1H), 8.27 (d, 1H), 7.80 – 7.74 (m, 2H), 7.68 (dd, 1H), 7.40 – 7.35 (m, 2H), 6.83 (d, 1H), 5.31 – 5.00 (m, 2H), 4.55 – 4.41 (m, 3H), 4.30 – 4.12 (m, 3H), 3.29 – 3.25 (m, 1H), 2.98 (s, 6H), 2.76 (d, 3H), 1.42 (t, 3H).

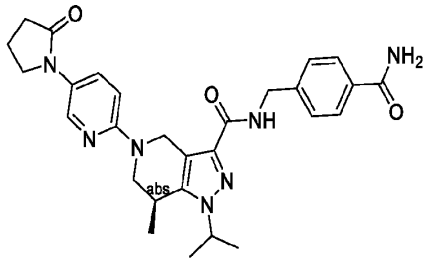
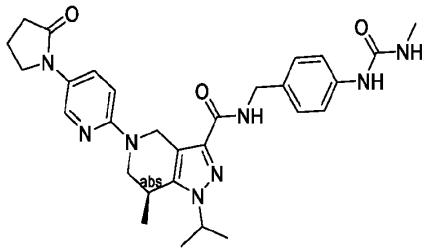
469	Ex. 469		*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	545.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, 1H), 7.40 (dd, 1H), 7.37 – 7.33 (m, 2H), 7.31 – 7.27 (m, 2H), 7.16 (t, 1H), 6.79 (d, 1H), 6.32 (s, 1H), 4.70 (s, 2H), 4.55 (d, 2H), 4.42 – 4.31 (m, 1H), 4.08 (t, 2H), 3.93 – 3.76 (m, 2H), 3.12 – 3.00 (m, 7H), 2.86 – 2.75 (m, 3H), 2.71 – 2.60 (m, 1H), 1.44 (d, 6H).
470	Ex. 128		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	602.6; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.47 (s, 1H), 8.38 – 8.34 (m, 1H), 8.26 – 8.23 (m, 1H), 7.66 – 7.63 (m, 1H), 7.41 – 7.37 (m, 2H), 7.21 – 7.17 (m, 2H), 6.92 – 6.88 (m, 1H), 5.12 – 5.08 (m, 1H), 4.58 – 4.51 (m, 1H), 4.44 – 4.30 (m, 3H), 4.27 – 4.22 (m, 1H), 3.42 (s, 4H), 3.37 – 3.35 (m, 1H), 3.27 – 3.21 (m, 1H), 2.99 (s, 6H), 2.31 (s, 4H), 2.20 (s, 3H), 1.45 – 1.40 (m, 6H), 1.22 – 1.18 (m, 3H).

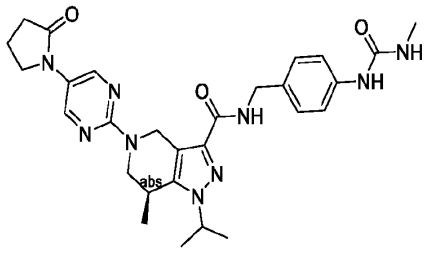
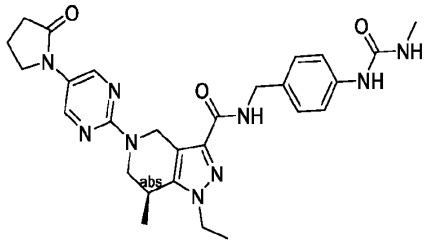
471	Ex. 127		(*S*)-*N*-(4-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	572.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.57 (t, 1H), 8.20 (d, 1H), 7.60 (dd, 1H), 7.45 – 7.40 (m, 2H), 7.34 – 7.29 (m, 2H), 6.85 (d, 1H), 5.06 (d, 1H), 4.57 – 4.35 (m, 4H), 4.20 (d, 1H), 3.30 – 3.27 (m, 4H), 3.23 – 3.16 (m, 1H), 2.94 (s, 6H), 2.01 (s, 3H), 1.40 (dd, 6H), 1.16 (d, 3H).
472	Ex. 113		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	549.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.39 (t, 1H), 8.23 (s, 2H), 7.63 (dd, 1H), 7.43 – 7.35 (m, 2H), 7.21 – 7.14 (m, 2H), 6.89 (d, 1H), 5.67 (d, 1H), 5.08 (d, 1H), 4.94 – 4.88 (m, 1H), 4.78 – 4.67 (m, 1H), 4.46 – 4.31 (m, 3H), 4.14 (dd, 1H), 3.70 (dd, 1H), 2.98 (s, 6H), 2.91 (s, 6H), 1.43 (d, 6H).

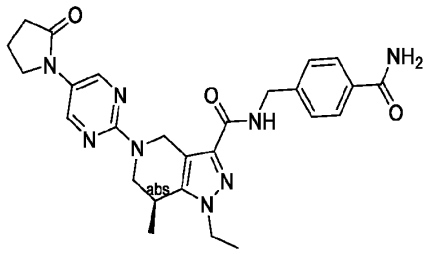
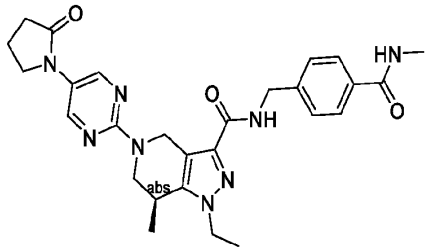
473	Ex. 537		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	556.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.43 (d, 1H), 8.35 (t, 1H), 8.23 (s, 1H), 7.84 (dd, 1H), 7.41 – 7.36 (m, 1H), 7.21 – 7.15 (m, 3H), 6.99 – 6.90 (m, 2H), 5.08 (d, 1H), 4.59 – 4.18 (m, 6H), 3.71 (s, 3H), 3.40 – 3.34 (m, 1H), 3.26 – 3.19 (m, 1H), 2.90 (m, 6H), 1.42 (dd, 6H), 1.22 (d, 3H).
474 ^	Ex. 113		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	549.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.37 (t, 1H), 8.23 – 8.18 (m, 2H), 7.60 (dd, 1H), 7.38 – 7.33 (m, 2H), 7.17 – 7.12 (m, 2H), 6.86 (d, 1H), 5.65 (d, 1H), 5.05 (d, 1H), 4.90 – 4.85 (m, 1H), 4.76 – 4.64 (m, 1H), 4.42 – 4.29 (m, 3H), 4.11 (dd, 1H), 3.66 (dd, 1H), 2.94 (s, 6H), 2.88 (s, 6H), 1.40 (d, 6H).

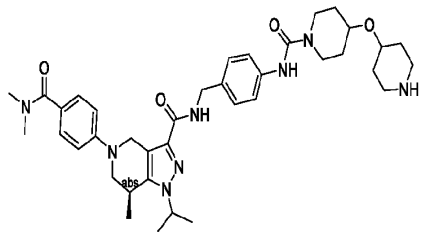
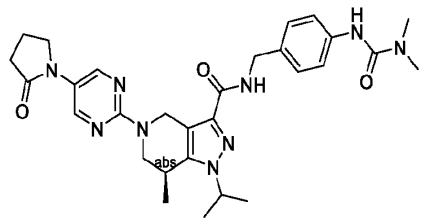
475 ^	Ex. 113		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	549.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.37 (t, 1H), 8.24 – 8.19 (m, 2H), 7.60 (dd, 1H), 7.39 – 7.33 (m, 2H), 7.17 – 7.11 (m, 2H), 6.86 (d, 1H), 5.71 – 5.59 (m, 1H), 5.06 (d, 1H), 4.92 – 4.83 (m, 1H), 4.75 – 4.64 (m, 1H), 4.44 – 4.29 (m, 3H), 4.12 (dd, 1H), 3.66 (dd, 1H), 2.95 (s, 6H), 2.88 (s, 6H), 1.40 (d, 6H).
476	Ex. 77		(*S*)-1-ethyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	531.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.44 – 8.38 (m, 2H), 8.27 (d, 1H), 7.87 (dd, 1H), 7.32 – 7.27 (m, 2H), 7.17 – 7.13 (m, 2H), 6.88 (d, 1H), 5.94 (q, 1H), 4.88 (d, 1H), 4.39 – 4.02 (m, 6H), 3.82 – 3.72 (m, 2H), 3.42 – 3.36 (m, 1H), 3.21 – 3.13 (m, 1H), 2.61 (d, 3H), 2.42 (t, 2H), 2.10 – 1.99 (m, 2H), 1.37 (t, 3H), 1.20 (d, 3H).

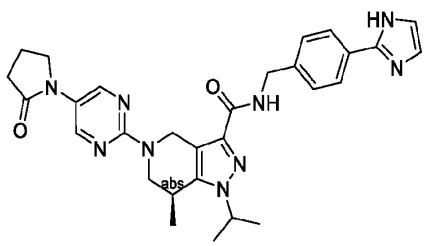
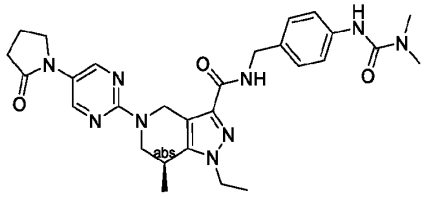
477	Ex. 127		(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	608.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.53 – 8.41 (m, 3H), 8.23 (s, 1H), 7.93 – 7.68 (m, 2H), 7.41 – 7.27 (m, 3H), 7.20 – 7.12 (m, 2H), 6.93 (d, 1H), 5.10 (d, 1H), 5.01 – 4.78 (m, 4H), 4.43 – 4.25 (m, 4H), 4.18 – 4.04 (m, 2H), 3.49 – 3.37 (m, 1H), 3.27 – 3.19 (m, 1H), 2.90 (s, 6H), 1.39 (t, 3H), 1.22 (d, 3H).
478	Ex. 530		(*S*)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	530.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.53 (t, 1H), 8.40 – 8.33 (m, 1H), 8.30 – 8.24 (m, 1H), 7.87 (dd, 1H), 7.80 – 7.74 (m, 2H), 7.41 – 7.34 (m, 2H), 6.89 (d, 1H), 4.94 (d, 1H), 4.59 – 4.28 (m, 4H), 4.16 (d, 1H), 3.81 – 3.73 (m, 2H), 3.26 – 3.16 (m, 2H), 2.77 (d, 3H), 2.46 – 2.39 (m, 2H), 2.11 – 1.99 (m, 2H), 1.43 (dd, 6H), 1.21 (d, 3H).

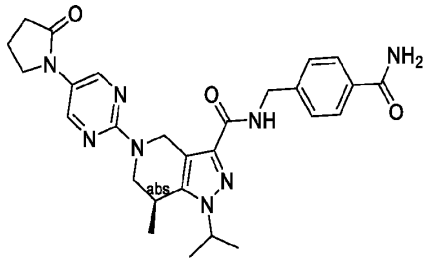
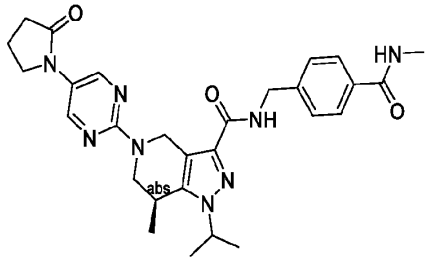
479	39[l]		(*S*)-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	516.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.53 (t, 1H), 8.28 (d, 1H), 7.94 – 7.79 (m, 4H), 7.41 – 7.28 (m, 3H), 6.89 (d, 1H), 4.94 (d, 1H), 4.60 – 4.25 (m, 4H), 4.16 (d, 1H), 3.77 (t, 2H), 3.27 – 3.16 (m, 2H), 2.46 – 2.38 (m, 2H), 2.10 – 2.01 (m, 2H), 1.43 (dd, 6H), 1.21 (d, 3H).
480	Ex. 39[l]		(*S*)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	545.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.44 (s, 1H), 8.35 – 8.27 (m, 2H), 7.88 (dd, 1H), 7.36 – 7.28 (m, 2H), 7.20 – 7.13 (m, 2H), 6.89 (d, 1H), 5.95 (q, 1H), 4.94 (d, 1H), 4.60 – 4.46 (m, 1H), 4.37 – 4.25 (m, 3H), 4.16 (d, 1H), 3.85 – 3.73 (m, 2H), 3.28 – 3.16 (m, 2H), 2.62 (d, 3H), 2.47 – 2.39 (m, 2H), 2.12 – 2.00 (m, 2H), 1.42 (dd, 6H), 1.20 (d, 3H).

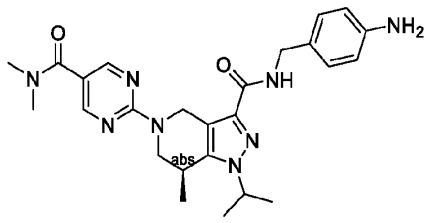
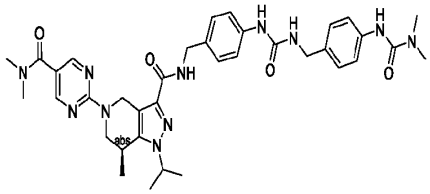
481	Ex. 127		(*S*)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	546.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (s, 2H), 8.44 (s, 1H), 8.32 (t, 1H), 7.34 – 7.28 (m, 2H), 7.19 – 7.14 (m, 2H), 5.98 – 5.89 (m, 1H), 5.35 (d, 1H), 4.71 – 4.62 (m, 1H), 4.57 – 4.44 (m, 1H), 4.39 – 4.19 (m, 3H), 3.80 – 3.73 (m, 2H), 3.26 – 3.15 (m, 2H), 2.61 (d, 2H), 2.46 – 2.39 (m, 3H), 2.12 – 1.99 (m, 2H), 1.41 (dd, 6H), 1.14 (d, 3H).
482	Ex. 127		(*S*)-1-ethyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	532.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (s, 2H), 8.45 – 8.39 (m, 2H), 7.33 – 7.28 (m, 2H), 7.19 – 7.12 (m, 2H), 5.94 (q, 1H), 5.29 (d, 1H), 4.59 (dd, 1H), 4.37 – 4.24 (m, 3H), 4.15 – 4.03 (m, 2H), 3.80 – 3.74 (m, 2H), 3.44 – 3.36 (m, 1H), 3.24 – 3.15 (m, 1H), 2.61 (d, 3H), 2.47 – 2.38 (m, 2H), 2.14 – 2.02 (m, 2H), 1.37 (t, 3H), 1.15 (d, 3H).

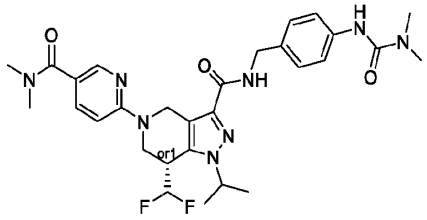
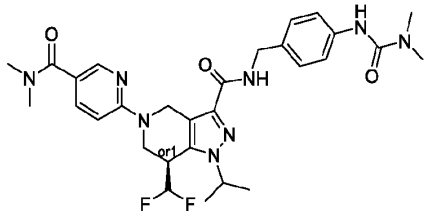
483	Ex. 127		(*S*)-*N*-(4-carbamoylbenzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	503.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.67 – 8.60 (m, 3H), 7.91 (s, 1H), 7.83 – 7.79 (m, 2H), 7.38 – 7.27 (m, 3H), 5.29 (d, 1H), 4.65 – 4.54 (m, 1H), 4.50 – 4.37 (m, 2H), 4.30 (d, 1H), 4.17 – 4.03 (m, 2H), 3.76 (t, 2H), 3.45 – 3.37 (m, 1H), 3.26 – 3.15 (m, 1H), 2.46 – 2.39 (m, 2H), 2.12 – 2.00 (m, 2H), 1.38 (t, 3H), 1.15 (d, 3H).
484	Ex. 127		(*S*)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	517.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.67 – 8.58 (m, 3H), 8.36 (q, 1H), 7.79 – 7.73 (m, 2H), 7.39 – 7.32 (m, 2H), 5.29 (d, 1H), 4.63 – 4.55 (m, 1H), 4.51 – 4.37 (m, 2H), 4.33 – 4.24 (m, 1H), 4.16 – 4.01 (m, 2H), 3.76 (t, 2H), 3.45 – 3.35 (m, 1H), 3.27 – 3.16 (m, 1H), 2.76 (d, 3H), 2.46 – 2.37 (m, 2H), 2.13 – 2.00 (m, 2H), 1.38 (t, 3H), 1.15 (d, 3H).

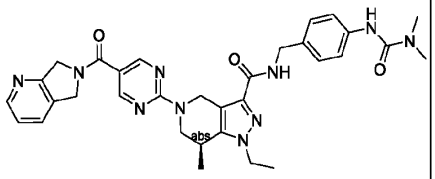
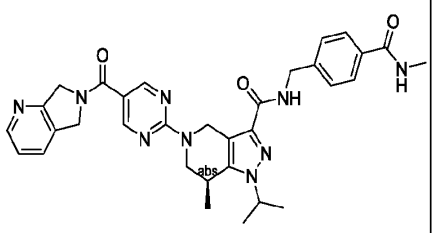
485	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-(piperidin-4-yloxy)piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	685.5; ^{1}H NMR* (400 MHz, $(CD_3)_2SO$) δ 8.70 – 8.50 (m, 2H), 8.42 – 8.34 (m, 1H), 8.24 (t, 1H), 7.31 – 7.19 (m, 4H), 7.12 – 7.05 (m, 2H), 6.89 – 6.83 (m, 2H), 4.50 – 4.38 (m, 2H), 4.31 – 4.19 (m, 2H), 4.00 (d, 1H), 3.76 – 3.59 (m, 4H), 3.58 – 3.50 (m, 1H), 3.21 – 2.93 (m, 6H), 2.92 – 2.80 (m, 8H), 1.86 – 1.77 (m, 2H), 1.74 – 1.66 (m, 2H), 1.60 – 1.48 (m, 2H), 1.37 – 1.25 (m, 7H), 1.18 (d, 3H).
486	Ex. 127		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	560.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (s, 2H), 8.33 (t, 1H), 8.23 (s, 1H), 7.41 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 5.35 (d, 1H), 4.71 – 4.63 (m, 1H), 4.57 – 4.46 (m, 1H), 4.41 – 4.20 (m, 3H), 3.77 (t, 2H), 3.41 – 3.35 (m, 1H), 3.25 – 3.17 (m, 1H), 2.90 (s, 6H), 2.46 – 2.38 (m, 2H), 2.14 – 1.99 (m, 2H), 1.41 (dd, 6H), 1.14 (d, 3H).

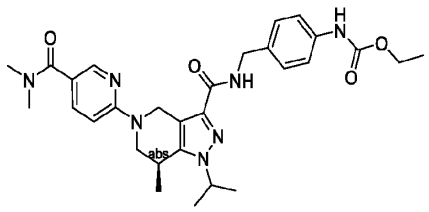
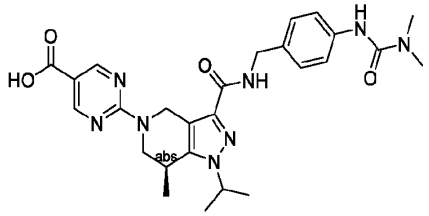
487	Ex. 127		(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	540.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 12.44 (s, 1H), 8.62 (s, 2H), 8.49 (t, 1H), 7.89 – 7.83 (m, 2H), 7.40 – 7.32 (m, 2H), 7.21 (s, 1H), 6.98 (s, 1H), 5.35 (d, 1H), 4.72 – 4.64 (m, 1H), 4.57 – 4.36 (m, 3H), 4.25 (d, 1H), 3.76 (t, 2H), 3.39 – 3.34 (m, 1H), 3.26 – 3.14 (m, 1H), 2.46 – 2.37 (m, 2H), 2.15 – 2.00 (m, 2H), 1.46 – 1.34 (m, 6H), 1.14 (d, 3H).
488	Ex. 127		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	546.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.63 (s, 2H), 8.43 (t, 1H), 8.22 (s, 1H), 7.41 – 7.35 (m, 2H), 7.20 – 7.13 (m, 2H), 5.30 (d, 1H), 4.60 (dd, 1H), 4.39 – 4.25 (m, 3H), 4.14 – 4.02 (m, 2H), 3.80 – 3.74 (m, 2H), 3.45 – 3.36 (m, 1H), 3.25 – 3.14 (m, 1H), 2.90 (s, 6H), 2.46 – 2.39 (m, 2H), 2.13 – 2.00 (m, 2H), 1.38 (t, 3H), 1.15 (d, 3H).

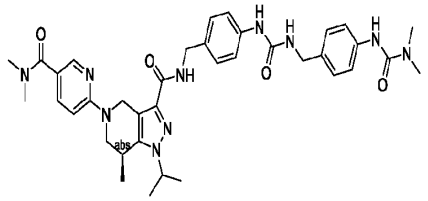
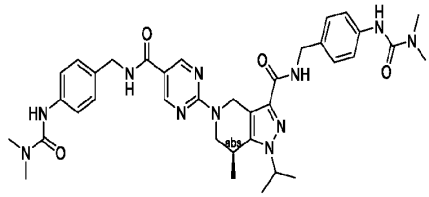
489	Ex. 127		(*S*)-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	517.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (s, 2H), 8.53 (t, 1H), 7.91 (s, 1H), 7.84 – 7.79 (m, 2H), 7.41 – 7.33 (m, 2H), 7.30 (s, 1H), 5.34 (d, 1H), 4.72 – 4.63 (m, 1H), 4.59 – 4.38 (m, 3H), 4.24 (d, 1H), 3.77 (t, 2H), 3.27 – 3.16 (m, 2H), 2.46 – 2.38 (m, 2H), 2.13 – 2.00 (m, 2H), 1.42 (dd, 6H), 1.14 (d, 3H).
490	Ex. 127		(*S*)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	531.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.62 (s, 2H), 8.53 (t, 1H), 8.40 – 8.34 (m, 1H), 7.81 – 7.73 (m, 2H), 7.40 – 7.33 (m, 2H), 5.34 (d, 1H), 4.71 – 4.64 (m, 1H), 4.58 – 4.38 (m, 3H), 4.24 (d, 1H), 3.81 – 3.73 (m, 2H), 3.27 – 3.16 (m, 2H), 2.76 (d, 3H), 2.47 – 2.39 (m, 2H), 2.12 – 2.00 (m, 2H), 1.47 – 1.34 (m, 6H), 1.14 (d, 3H).

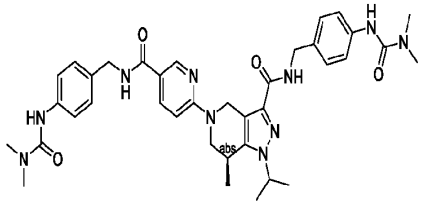
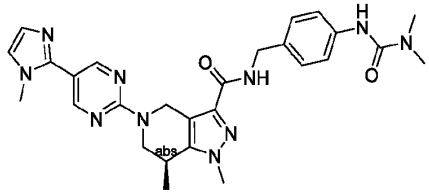
491	Ex. 126		(*S*)-*N*-(4-aminobenzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	477.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.47 (s, 2H), 8.10 (t, 1H), 6.98 – 6.91 (m, 2H), 6.49 – 6.41 (m, 2H), 5.42 (d, 1H), 4.90 (s, 2H), 4.74 – 4.65 (m, 1H), 4.52 – 4.41 (m, 1H), 4.31 – 4.12 (m, 3H), 3.23 – 3.17 (m, 1H), 3.01 – 2.88 (m, 7H), 1.39 – 1.30 (m, 6H), 1.12 – 1.07 (m, 3H).
492	Ex. 127		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3-(4-(3,3-dimethylureido)benzyl)ureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	696.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.48 (s, 2H), 8.43 (s, 1H), 8.31 (t, 1H), 8.20 (s, 1H), 7.39 – 7.32 (m, 2H), 7.32 – 7.26 (m, 2H), 7.19 – 7.07 (m, 4H), 6.43 (t, 1H), 5.43 (d, 1H), 4.75 – 4.68 (m, 1H), 4.54 – 4.43 (m, 1H), 4.37 – 4.23 (m, 3H), 4.16 (d, 2H), 3.29 – 3.21 (m, 1H), 2.96 (s, 6H), 2.89 – 2.82 (m, 7H), 1.38 (dd, 6H), 1.11 (d, 3H).

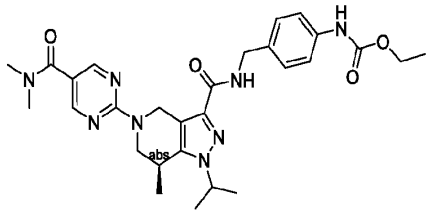
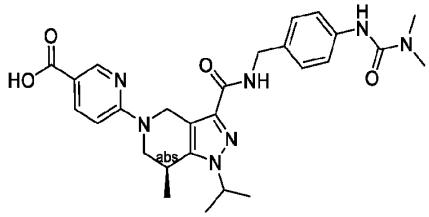
493 ^	Ex. 39		*rel*-(*R* or *S*)-7-(difluoromethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	583.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.27 (d, 1H), 8.22 (s, 1H), 7.68 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.20 – 7.14 (m, 2H), 6.83 (d, 1H), 6.25 – 5.89 (m, 1H), 5.10 – 4.98 (m, 2H), 4.71 – 4.56 (m, 1H), 4.42 – 4.16 (m, 3H), 3.91 – 3.79 (m, 1H), 3.23 – 3.17 (m, 1H), 2.98 (s, 6H), 2.90 (s, 6H), 1.46 – 1.35 (m, 6H).
494 ^	Ex. 39		*rel*-(*R* or *S*)-7-(difluoromethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	583.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.47 (t, 1H), 8.26 (d, 1H), 8.22 (s, 1H), 7.68 (dd, 1H), 7.41 – 7.34 (m, 2H), 7.20 – 7.14 (m, 2H), 6.82 (d, 1H), 6.27 – 5.83 (m, 1H), 5.09 – 4.96 (m, 2H), 4.67 – 4.57 (m, 1H), 4.41 – 4.19 (m, 3H), 3.92 – 3.79 (m, 1H), 3.23 – 3.15 (m, 1H), 2.97 (s, 6H), 2.89 (s, 6H), 1.48 – 1.34 (m, 6H).

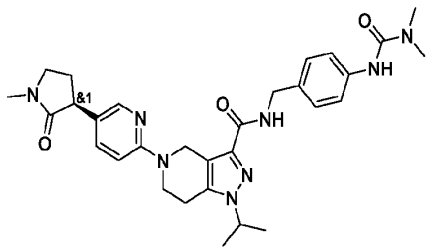
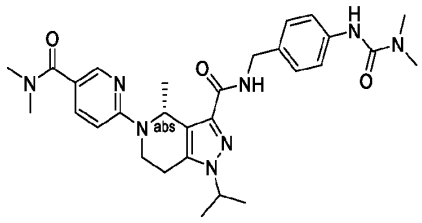
495	Ex. 127		(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	609.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.74 (d, 2H), 8.49 – 8.41 (m, 2H), 8.22 (s, 1H), 7.86 – 7.68 (m, 1H), 7.40 – 7.35 (m, 2H), 7.34 – 7.27 (m, 1H), 7.19 – 7.13 (m, 2H), 5.45 (d, 1H), 5.05 – 4.66 (m, 5H), 4.46 – 4.24 (m, 3H), 4.16 – 4.04 (m, 2H), 3.55 – 3.46 (m, 1H), 2.91 – 2.85 (m, 7H), 1.38 (t, 3H), 1.17 (d, 3H).
496	Ex. 127		(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	594.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.76 – 8.69 (m, 2H), 8.58 – 8.52 (m, 1H), 8.48 – 8.43 (m, 1H), 8.39 – 8.34 (m, 1H), 7.86 – 7.68 (m, 3H), 7.40 – 7.27 (m, 3H), 5.49 (d, 1H), 5.06 – 4.73 (m, 5H), 4.58 – 4.27 (m, 4H), 3.50 – 3.39 (m, 2H), 2.76 (d, 3H), 1.43 (dd, 6H), 1.16 (d, 3H).

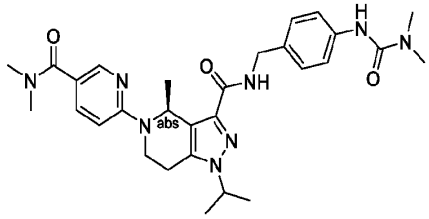
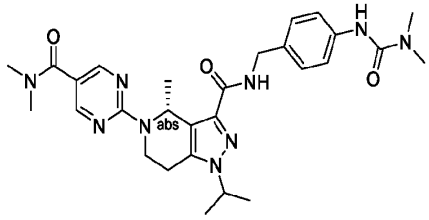
497	Ex. 236		ethyl (*S*)-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate	548.4 ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.54 (s, 1H), 8.36 (t, 1H), 8.23 (d, 1H), 7.62 (dd, 1H), 7.37 (d, 2H), 7.21 (d, 2H), 6.87 (d, 1H), 5.07 (d, 1H), 4.57 – 4.47 (m, 1H), 4.45 – 4.27 (m, 3H), 4.25 – 4.17 (m, 1H), 4.09 (q, 2H), 3.26 – 3.14 (m, 2H), 2.96 (s, 6H), 1.40 (dd, 6H), 1.24 – 1.16 (m, 6H).
498	Ex. 498		(*S*)-2-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyrimidine-5-carboxylic acid	521.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.80 (s, 2H), 8.36 (t, 1H), 8.24 (s, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.14 (m, 2H), 5.54 (d, 1H), 4.81 (d, 1H), 4.57 – 4.46 (m, 1H), 4.40 – 4.27 (m, 3H), 3.49 – 3.41 (m, 1H), 3.32 – 3.22 (m, 1H), 2.94 – 2.86 (m, 6H), 1.41 (dd, 6H), 1.13 (d, 3H).

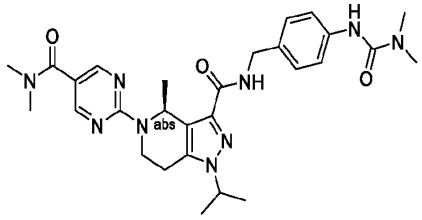
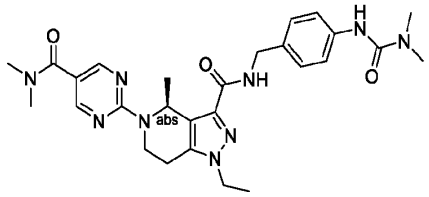
499	Ex. 127		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-(4-(3,3-dimethylureido)benzyl)ureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	695.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.48 (s, 1H), 8.34 (t, 1H), 8.26 – 8.21 (m, 2H), 7.64 (dd, 1H), 7.42 – 7.37 (m, 2H), 7.36 – 7.31 (m, 2H), 7.21 – 7.11 (m, 4H), 6.89 (d, 1H), 6.48 (t, 1H), 5.09 (d, 1H), 4.58 – 4.48 (m, 1H), 4.46 – 4.16 (m, 7H), 3.27 – 3.17 (m, 1H), 3.03 – 2.94 (m, 6H), 2.93 – 2.84 (m, 6H), 1.42 (dd, 6H), 1.20 (d, 3H).
500	Ex. 395		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	696.5; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.88 – 8.79 (m, 3H), 8.35 (t, 1H), 8.23 – 8.20 (m, 2H), 7.41 – 7.35 (m, 4H), 7.19 – 7.12 (m, 4H), 5.49 (d, 1H), 4.79 (d, 1H), 4.55 – 4.45 (m, 1H), 4.42 – 4.27 (m, 5H), 3.45 – 3.37 (m, 1H), 3.27 – 3.20 (m, 1H), 2.93 – 2.83 (m, 12H), 1.41 (dd, 6H), 1.12 (d, 3H).

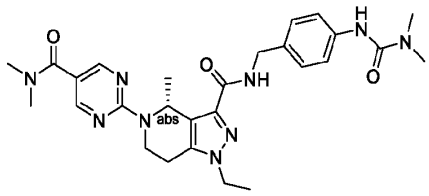
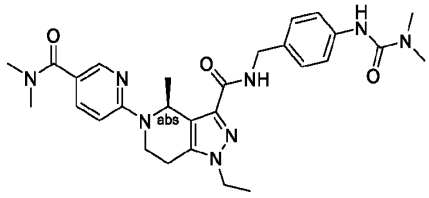
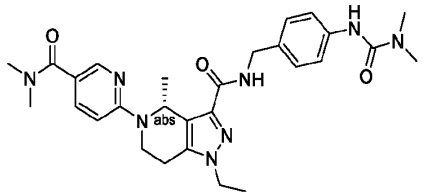
501	Ex. 127		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	695.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.75 (t, 1H), 8.65 (d, 1H), 8.36 (t, 1H), 8.25 – 8.19 (m, 2H), 8.01 (dd, 1H), 7.41 – 7.34 (m, 4H), 7.21 – 7.11 (m, 4H), 6.91 (d, 1H), 5.13 (d, 1H), 4.59 – 4.44 (m, 2H), 4.41 – 4.22 (m, 5H), 3.26 – 3.19 (m, 2H), 2.92 – 2.84 (m, 12H), 1.42 (dd, 6H), 1.18 (d, 3H).
502	Ex. 127		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	529.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (s, 2H), 8.49 – 8.44 (m, 1H), 8.22 – 8.19 (m, 1H), 7.85 – 7.81 (m, 1H), 7.39 – 7.33 (m, 2H), 7.16 – 7.07 (m, 3H), 5.39 – 5.30 (m, 1H), 4.64 – 4.57 (m, 1H), 4.43 – 4.27 (m, 3H), 3.80 (s, 3H), 3.64 (s, 3H), 3.54 – 3.44 (m, 2H), 2.89 (s, 6H), 1.16 (d, 3H).

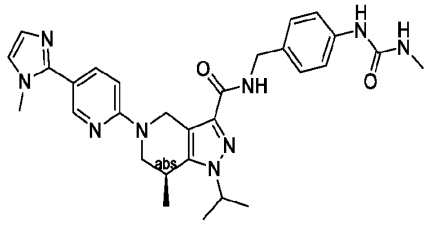
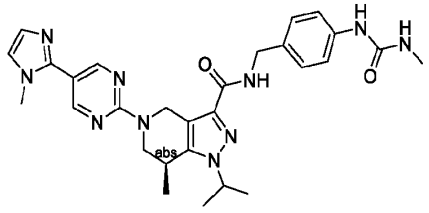
503	Ex. 236		ethyl (*S*)-(4-((5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate	549.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.54 (s, 1H), 8.51 (s, 2H), 8.37 (t, 1H), 7.38 (d, 2H), 7.24 – 7.20 (m, 2H), 5.46 (d, 1H), 4.78 – 4.69 (m, 1H), 4.57 – 4.46 (m, 1H), 4.41 – 4.27 (m, 3H), 4.10 (q, 2H), 3.47 – 3.36 (m, 1H), 3.26 – 3.23 (m, 1H), 2.99 (s, 6H), 1.41 (dd, 6H), 1.22 (t, 3H), 1.14 (d, 3H).
504	Ex. 498		(*S*)-6-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinic acid	520.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.58 – 8.54 (m, 1H), 8.41 (t, 1H), 8.25 (s, 1H), 8.08 – 8.01 (m, 1H), 7.42 – 7.37 (m, 2H), 7.20 – 7.15 (m, 2H), 7.14 – 7.09 (m, 1H), 5.15 (d, 1H), 4.60 – 4.46 (m, 2H), 4.40 – 4.27 (m, 3H), 3.51 – 3.43 (m, 1H), 3.34 – 3.25 (m, 1H), 2.90 (s, 6H), 1.45 – 1.39 (m, 6H), 1.20 (d, 3H).

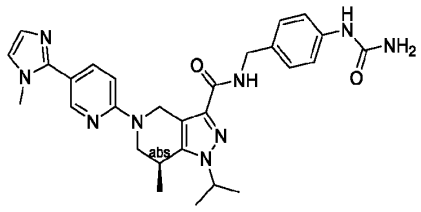
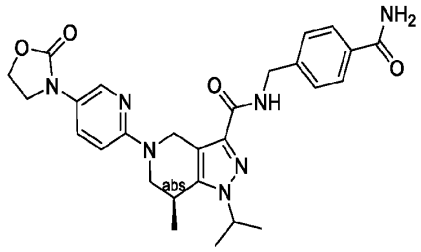
505	Ex. 469[n]		*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, 1H), 7.43 – 7.39 (m, 1H), 7.38 – 7.33 (m, 2H), 7.32 – 7.28 (m, 2H), 7.18 – 7.11 (m, 1H), 6.78 (d, 1H), 6.29 (s, 1H), 4.69 (s, 2H), 4.56 (d, 2H), 4.42 – 4.31 (m, 1H), 4.09 (t, 2H), 3.63 – 3.48 (m, 2H), 3.37 (s, 3H), 3.17 – 3.07 (m, 1H), 3.03 (s, 6H), 2.83 – 2.75 (m, 3H), 2.68 – 2.59 (m, 1H), 1.44 (d, 6H).
506 ^	Ex. 113[f]		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.31 (t, 1H), 8.23 (s, 2H), 7.64 – 7.58 (m, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 6.87 – 6.82 (m, 1H), 5.83 – 5.72 (m, 1H), 4.67 – 4.56 (m, 1H), 4.52 – 4.24 (m, 3H), 3.40 – 3.34 (m, 1H), 2.97 (s, 6H), 2.91 (d, 6H), 2.85 – 2.69 (m, 2H), 1.43 (d, 6H), 1.35 (d, 3H).

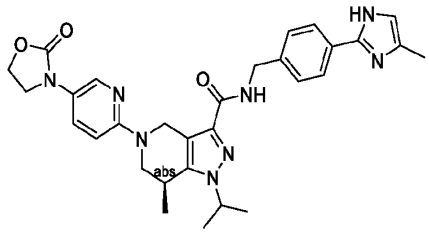
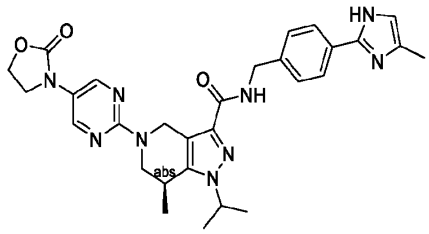
507 ^	Ex. 113[f]		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.31 (t, 1H), 8.24 – 8.21 (m, 2H), 7.62 (dd, 1H), 7.42 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 6.85 (d, 1H), 5.84 – 5.72 (m, 1H), 4.67 – 4.55 (m, 1H), 4.52 – 4.26 (m, 3H), 3.39 – 3.34 (m, 1H), 2.97 (s, 6H), 2.91 (s, 6H), 2.86 – 2.64 (m, 2H), 1.43 (d, 6H), 1.35 (d, 3H).
508 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.51 (s, 2H), 8.32 (t, 1H), 8.23 (s, 1H), 7.42 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 6.09 (q, 1H), 5.00 (dd, 1H), 4.53 – 4.26 (m, 3H), 3.30 – 3.23 (m, 1H), 2.99 (s, 6H), 2.93 – 2.87 (m, 6H), 2.86 – 2.70 (m, 2H), 1.46 – 1.40 (m, 6H), 1.35 (d, 3H).

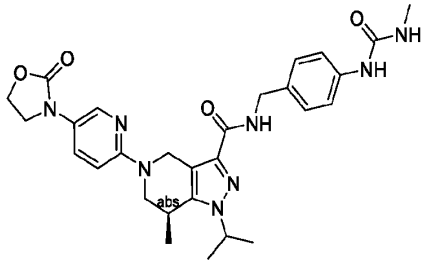
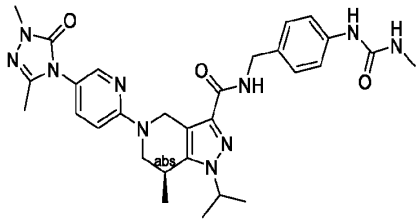
509 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.4; 1H NMR (400 MHz, $(CD_3)_2SO$) δ 8.51 (s, 2H), 8.32 (t, 1H), 8.23 (s, 1H), 7.42 – 7.37 (m, 2H), 7.19 – 7.14 (m, 2H), 6.09 (q, 1H), 5.00 (dd, 1H), 4.53 – 4.25 (m, 3H), 3.31 – 3.26 (m, 1H), 2.99 (s, 6H), 2.92 – 2.89 (m, 6H), 2.89 – 2.69 (m, 2H), 1.46 – 1.41 (m, 6H), 1.35 (d, 3H).
510 ^	Ex. 113		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	534.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.51 (s, 2H), 8.40 (t, 1H), 8.22 (s, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.14 (m, 2H), 6.13 – 6.07 (m, 1H), 5.05 – 4.95 (m, 1H), 4.43 – 4.24 (m, 3H), 4.12 – 3.99 (m, 2H), 2.99 (s, 6H), 2.91 (s, 6H), 2.87 – 2.70 (m, 2H), 1.44 (d, 3H), 1.32 (t, 3H).

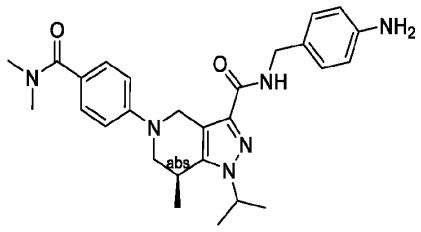
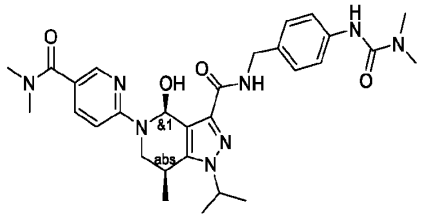
511 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	534.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.52 (s, 2H), 8.41 (t, 1H), 8.26 – 8.20 (m, 1H), 7.42 – 7.37 (m, 2H), 7.20 – 7.14 (m, 2H), 6.10 (q, 1H), 5.06 – 4.97 (m, 1H), 4.44 – 4.25 (m, 3H), 4.12 – 4.00 (m, 2H), 2.99 (s, 6H), 2.91 (s, 6H), 2.88 – 2.71 (m, 2H), 1.44 (d, 3H), 1.33 (t, 3H).
512 ^	Ex. 537		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.42 – 8.36 (m, 1H), 8.24 – 8.20 (m, 2H), 7.64 – 7.59 (m, 1H), 7.41 – 7.36 (m, 2H), 7.19 – 7.13 (m, 2H), 6.87 – 6.83 (m, 1H), 5.86 – 5.74 (m, 1H), 4.65 – 4.56 (m, 1H), 4.42 – 4.23 (m, 3H), 4.10 – 4.01 (m, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.79 – 2.71 (m, 2H), 1.43 (d, 3H), 1.33 (t, 3H).
513 ^	Ex. 537		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.39 (t, 1H), 8.24 – 8.20 (m, 2H), 7.62 (dd, 1H), 7.42 – 7.35 (m, 2H), 7.16 (d, 2H), 6.85 (d, 1H), 5.85 – 5.76 (m, 1H), 4.64 – 4.56 (m, 1H), 4.43 – 4.25 (m, 3H), 4.10 – 4.01 (m, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.81 – 2.72 (m, 2H), 1.43 (d, 3H), 1.32 (t, 3H).

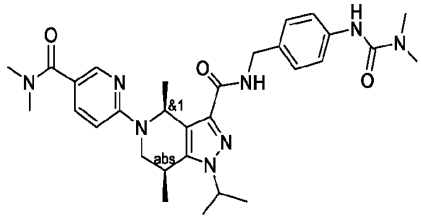
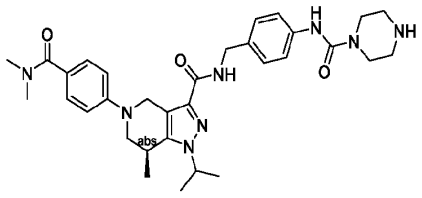
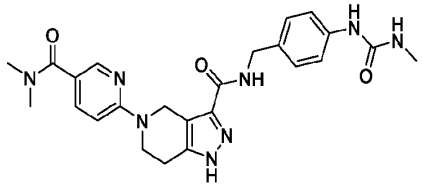
514	Ex. 18[f]		(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	542.3
515	Ex. 515		(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	543.5; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.77 (s, 1H), 8.44 (s, 1H), 8.38 (t, 1H), 7.81 – 7.77 (m, 2H), 7.34 – 7.30 (m, 2H), 7.19 – 7.15 (m, 2H), 5.97 – 5.93 (m, 1H), 5.55 (d, 1H), 4.82 (d, 1H), 4.57 – 4.50 (m, 1H), 4.41 – 4.28 (m, 3H), 3.87 – 3.85 (m, 3H), 3.50 – 3.47 (m, 2H), 3.34 – 3.28 (m, 1H), 2.62 (d, 3H), 1.43 (dd, 6H), 1.16 (d, 3H).

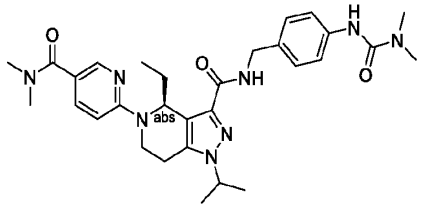
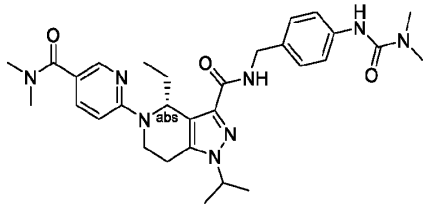
516	Ex. 18[f]		(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.4
517	Ex. 77		*(S)-N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	518.4

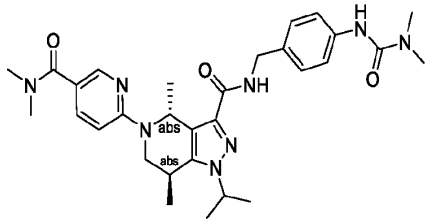
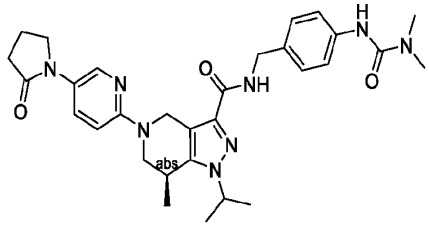
518	Ex. 77		(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1*H*-imidazol-2-yl)benzyl)-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	555.3
519	Ex. 127		(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1*H*-imidazol-2-yl)benzyl)-5-(5-(2-oxooxazolidin-3-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	556.3

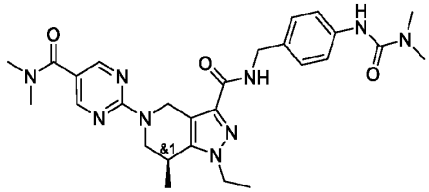
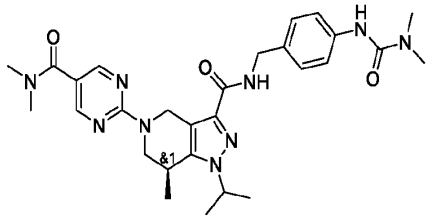
520	Ex. 127		(*S*)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	547.5
521	Ex. 127		(*S*)-5-(5-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.5

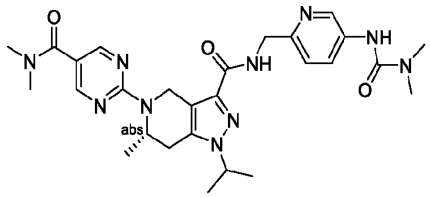
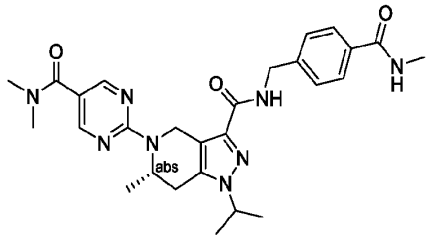
522	Ex. 2[l]		(*S*)-*N*-(4-aminobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	475.3
523	Ex. 523		(4*RS*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4-hydroxy-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.61 (t, 1H), 8.28 – 8.22 (m, 2H), 7.71 – 7.63 (m, 1H), 7.44 – 7.38 (m, 2H), 7.23 – 7.16 (m, 2H), 7.10 – 7.01 (m, 1H), 6.62 (s, 1H), 5.98 – 5.95 (m, 1H), 4.69 – 4.64 (m, 1H), 4.58 – 4.51 (m, 1H), 4.46 – 4.34 (m, 2H), 3.49 – 3.43 (m, 1H), 3.22 – 3.19 (m, 1H), 3.03 – 2.95 (m, 6H), 2.92 (s, 6H), 1.50 – 1.34 (m, 6H), 1.14 – 1.05 (m, 3H).

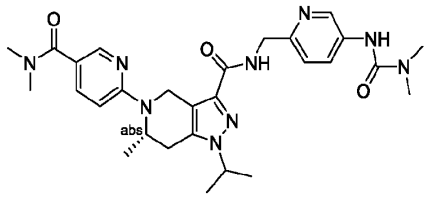
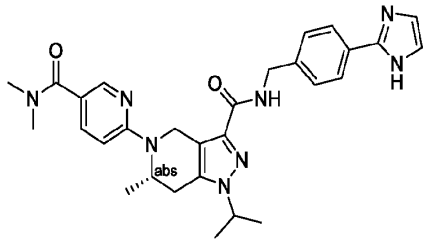
524	Ex. 524		(4*RS*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.4; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.34 (t, 1H), 8.24 – 8.19 (m, 2H), 7.64 (d, 1H), 7.41 – 7.36 (m, 2H), 7.20 – 7.15 (m, 2H), 6.93 (d, 1H), 5.73 (s, 1H), 4.52 – 4.46 (m, 2H), 4.43 – 4.37 (m, 1H), 4.34 – 4.27 (m, 1H), 3.42 (d, 1H), 3.23 – 3.16 (m, 1H), 2.98 (s, 6H), 2.90 (s, 6H), 1.43 – 1.36 (m, 9H), 1.13 (d, 3H).
525	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(piperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.4
526	Ex. 113		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	477.1

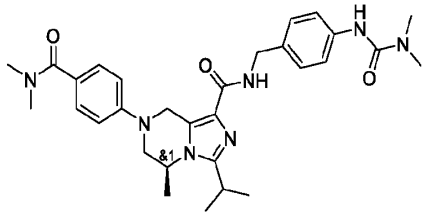
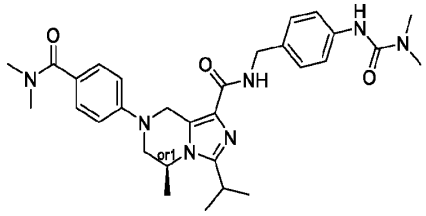
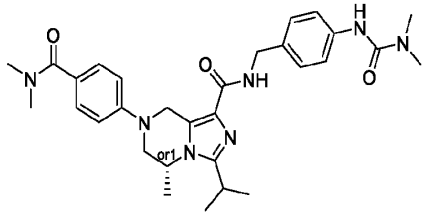
527 ^	Ex. 537		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.4
528 ^	Ex. 537		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.4

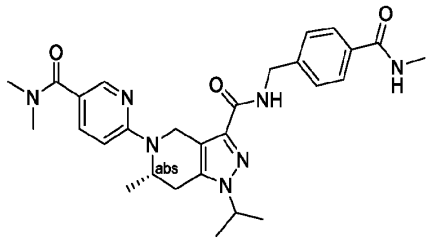
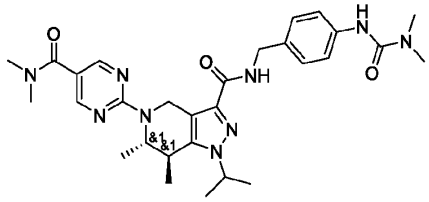
529 ^	Ex. 529		(4*R*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.2; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.29 (t, 1H), 8.21 – 8.17 (m, 2H), 7.57 (dd, 1H), 7.37 – 7.31 (m, 2H), 7.18 – 7.10 (m, 2H), 6.83 (d, 1H), 5.70 (s, 1H), 4.50 – 4.40 (m, 2H), 4.39 – 4.30 (m, 1H), 4.29 – 4.20 (m, 1H), 3.31 – 3.27 (m, 1H), 3.18 – 3.08 (m, 1H), 2.94 (s, 6H), 2.86 (s, 6H), 1.39 – 1.27 (m, 9H), 1.08 (d, 3H).
530	Ex. 530		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.2; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.33 (t, 1H), 8.29 (d, 1H), 8.23 (s, 1H), 7.88 (dd, 1H), 7.43 – 7.35 (m, 2H), 7.21 – 7.15 (m, 2H), 6.90 (d, 1H), 4.95 (d, 1H), 4.59 – 4.48 (m, 1H), 4.40 – 4.28 (m, 3H), 4.17 (d, 1H), 3.78 (t, 2H), 3.32 – 3.18 (m, 2H), 2.91 (s, 6H), 2.44 (t, 2H), 2.12 – 2.00 (m, 2H), 1.47 – 1.38 (m, 6H), 1.21 (d, 3H).

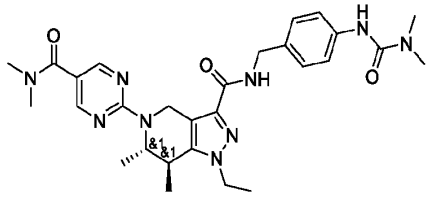
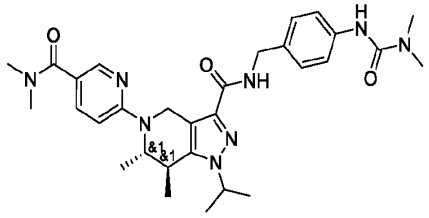
531	Ex. 125		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	534.5
532	Ex. 125		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.6

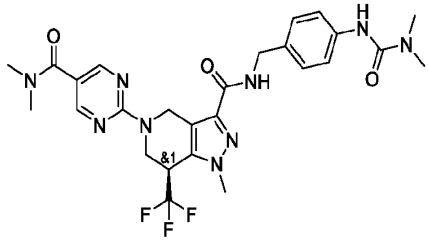
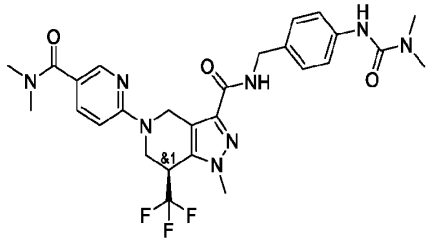
533	Ex. 125		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	549.7
534	Ex. 125[e]		(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-6-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	519.6

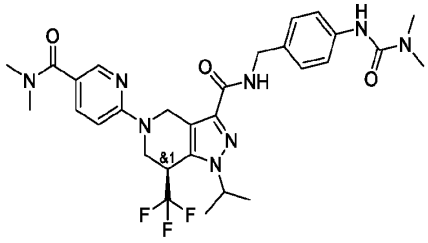
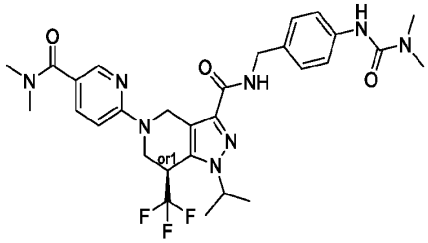
535	Ex. 125[e]		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.7
536	Ex. 125[e]		(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	527.6

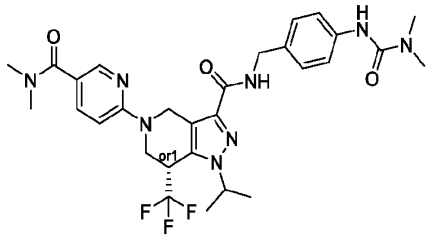
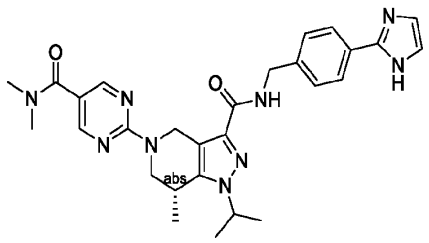
537	Ex. 537		*rac*-(*R*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	546.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.22 (s, 1H), 8.04 (t, 1H), 7.42 – 7.35 (m, 4H), 7.21 – 7.14 (m, 2H), 7.03 – 6.96 (m, 2H), 4.93 (d, 1H), 4.64 – 4.58 (m, 1H), 4.43 – 4.31 (m, 3H), 4.02 (d, 1H), 3.41 – 3.38 (m, 1H), 3.15 – 3.04 (m, 1H), 2.97 (s, 6H), 2.91 (s, 6H), 1.42 (d, 3H), 1.33 – 1.21 (m, 6H).
538 ^	Ex. 538		*rel*-(*R or S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	546.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.19 (s, 1H), 8.02 (t, 1H), 7.38 – 7.31 (m, 4H), 7.17 – 7.10 (m, 2H), 6.99 – 6.92 (m, 2H), 4.89 (d, 1H), 4.62 – 4.52 (m, 1H), 4.40 – 4.24 (m, 3H), 3.98 (d, 1H), 3.39 – 3.35 (m, 1H), 3.13 – 3.00 (m, 1H), 2.93 (s, 6H), 2.87 (s, 6H), 1.37 (d, 3H), 1.29 – 1.17 (m, 6H).
539 ^	Ex. 539		*rel*-(*R or S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide	546.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.19 (s, 1H), 8.02 (t, 1H), 7.38 – 7.28 (m, 4H), 7.18 – 7.07 (m, 2H), 7.00 – 6.91 (m, 2H), 4.88 (d, 1H), 4.60 – 4.52 (m, 1H), 4.38 – 4.26 (m, 3H), 3.97 (d, 1H), 3.42 – 3.38 (m, 1H), 3.11 – 3.00 (m, 1H), 2.92 (s, 6H), 2.86 (s, 6H), 1.36 (d, 3H), 1.27 – 1.17 (m, 6H).

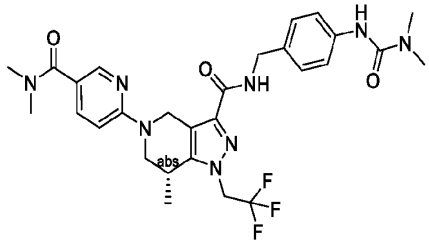
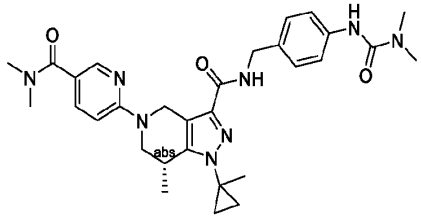
540	Ex. 125[e]		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-6-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	518.6
541	Ex. 4[k]		*rac*-(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	562.5

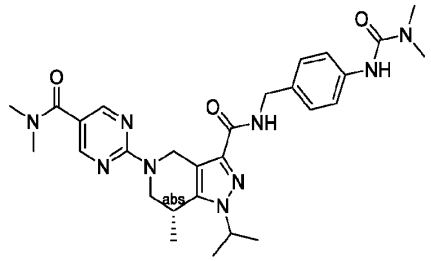
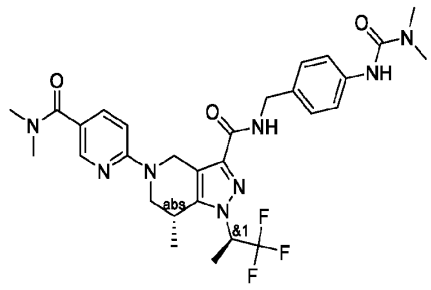
542	Ex. 23[k]		*rac*-(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.5
543	Ex. 127		*rac*-(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	561.5

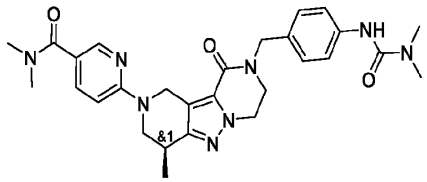
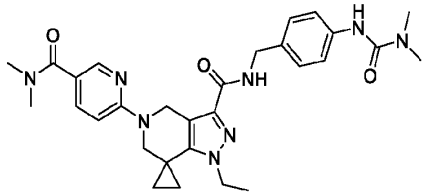
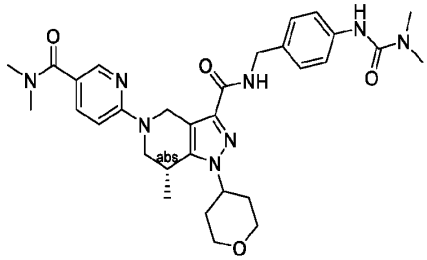
544	Ex. 39[f]		*rac-(R)*-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	574.7
545	Ex. 39[f]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.6

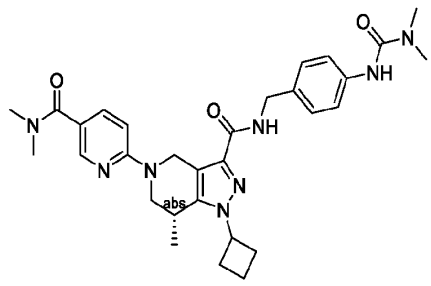
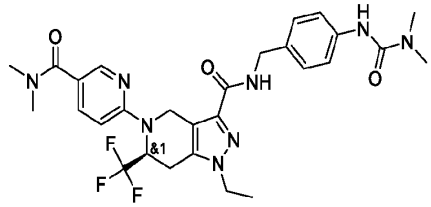
546	Ex. 546		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.7; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.57 – 8.52 (m, 1H), 8.29 – 8.27 (m, 1H), 8.26 – 8.22 (m, 1H), 7.72 – 7.67 (m, 1H), 7.43 – 7.38 (m, 2H), 7.23 – 7.15 (m, 2H), 6.87 – 6.82 (m, 1H), 4.72 – 4.65 (m, 1H), 4.56 – 4.50 (m, 1H), 4.41 – 4.33 (m, 2H), 4.31 – 4.26 (m, 1H), 4.13 – 4.07 (m, 1H), 3.22 – 3.15 (m, 2H), 2.99 (s, 6H), 2.93 – 2.90 (m, 6H), 1.48 – 1.40 (m, 6H).
547 ^	Ex. 547		*rel*-(*R or S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.3; ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 8.55 (t, 1H), 8.29 – 8.27 (m, 1H), 8.24 (s, 1H), 7.69 (dd, 1H), 7.42 – 7.38 (m, 2H), 7.21 – 7.17 (m, 2H), 6.84 (d, 1H), 4.72 – 4.65 (m, 1H), 4.57 – 4.49 (m, 1H), 4.42 – 4.32 (m, 2H), 4.31 – 4.25 (m, 1H), 4.16 – 4.06 (m, 1H), 3.30 – 3.27 (m, 1H), 3.18 – 3.15 (m, 1H), 2.99 (s, 6H), 2.91 (s, 6H), 1.44 (dd, 6H).

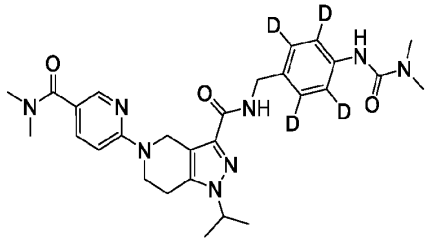
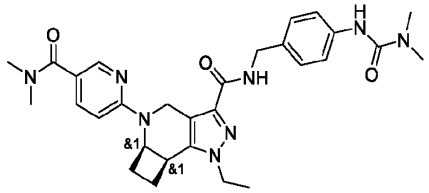
548 ^	Ex. 548		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.3
549 ^	Ex. 127		(*R*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	528.3

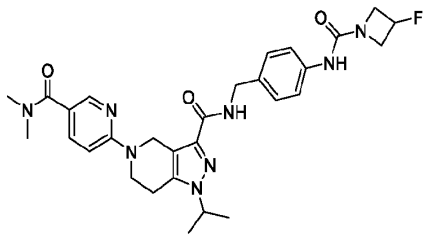
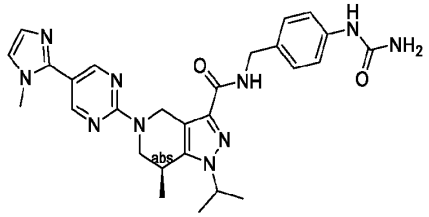
550 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.3
551 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3

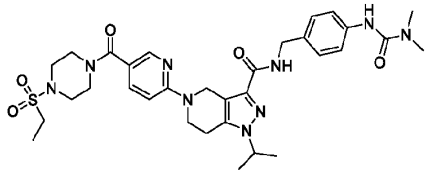
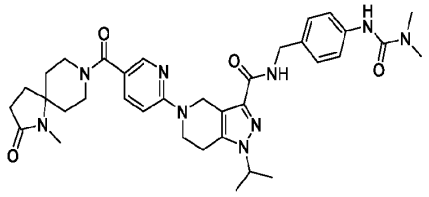
552 ^	Ex. 125		(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	548.3
553 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-((*RS*)-1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.3

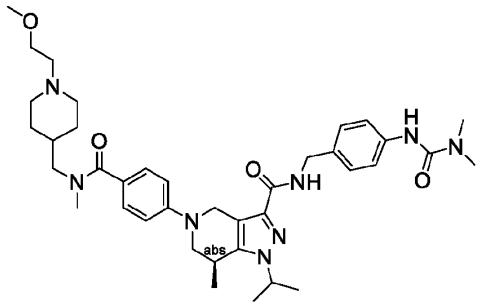
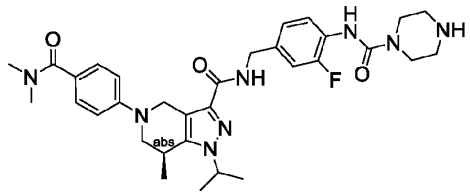
554	Ex. 252		*rac*-(*R*)-6-(9-(4-(3,3-dimethylureido)benzyl)-4-methyl-10-oxo-3,4,7,8,9,10-hexahydropyrido[4',3':3,4]pyrazolo[1,5-a]pyrazin-2(1*H*)-yl)-*N*,*N*-dimethylnicotinamide	531.4
555	Ex. 127		5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-ethyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide	545.6
556 ^	Ex. 113		(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	589.3

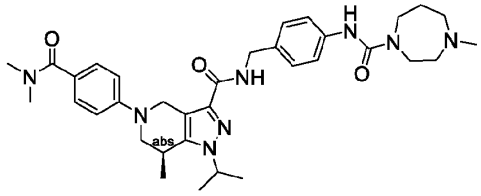
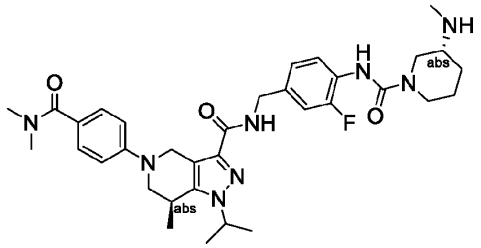
557 ^	Ex. 113		(*R*)-1-cyclobutyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3
558	Ex. 113[f]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.5

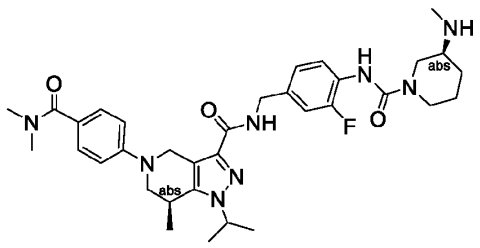
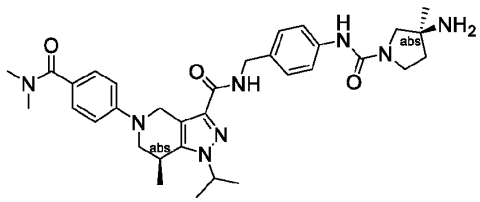
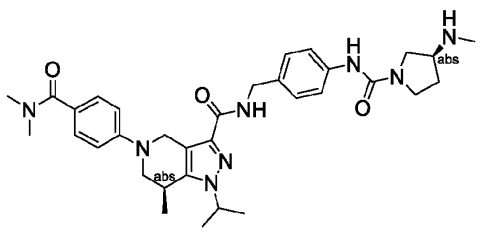
559	Ex. 561		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)2,3,5,6-d_4-benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	537.3; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.32 (t, 1H), 8.26 – 8.19 (m, 2H), 7.63 (dd, 1H), 6.88 (d, 1H), 4.75 (s, 2H), 4.55 – 4.43 (m, 1H), 4.35 (d, 2H), 3.95 (t, 2H), 2.97 (s, 6H), 2.91 (s, 6H), 2.82 (t, 2H), 1.39 (d, 6H)
560	Ex. 128		*rac*-(5*aR*,7*aS*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,5*a*,6,7,7*a*-hexahydro-1*H*-cyclobuta[b]pyrazolo[3,4-*d*]pyridine-3-carboxamide	545.4

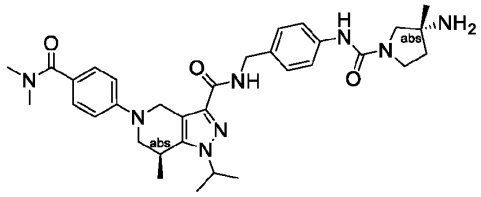
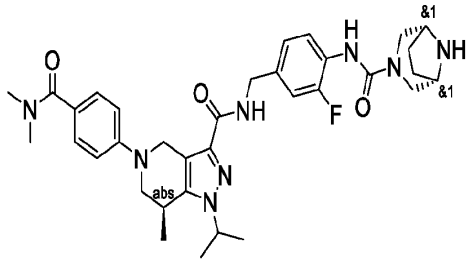
561	Ex. 136		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-fluoroazetidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	563.4
562	Ex. 515		(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	529.4

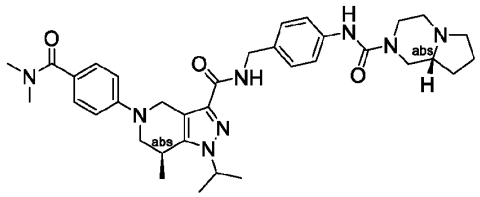
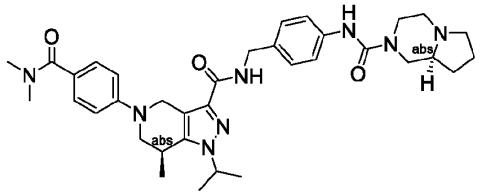
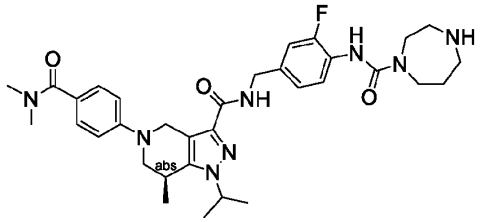
563	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-(ethylsulfonyl)piperazine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	666.4
564	Ex. 193		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-2-oxo-1,8-diazaspiro[4.5]decane-8-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	656.7

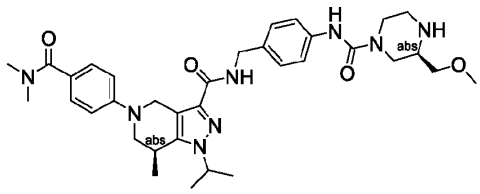
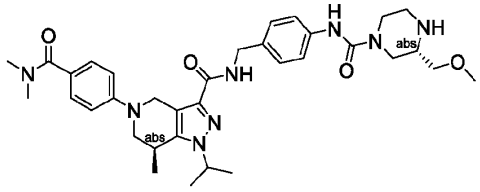
565	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(4-(((1-(2-methoxyethyl)piperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	688.3
566	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	605.4

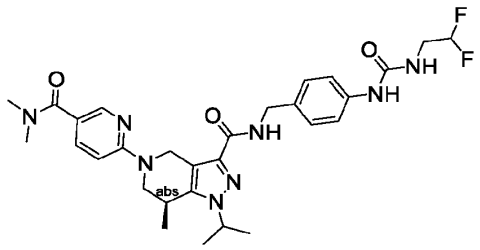
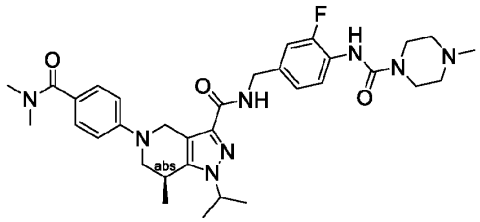
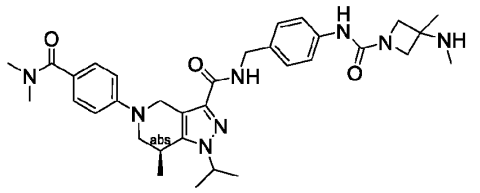
567	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.6
568	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-((*R*)-3-(methylamino)piperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.5

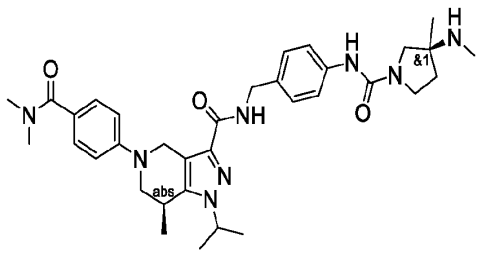
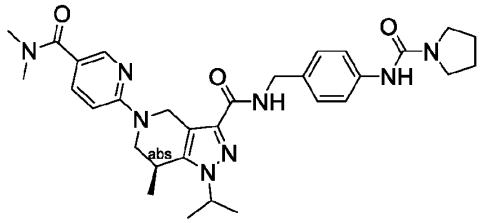
569	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-((*S*)-3-(methylamino)piperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.5
570	Ex. 485		(*S*)-*N*-(4-((*S*)-3-amino-3-methylpyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.5
571	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((S)-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-	601.5

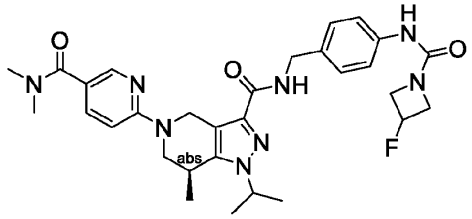
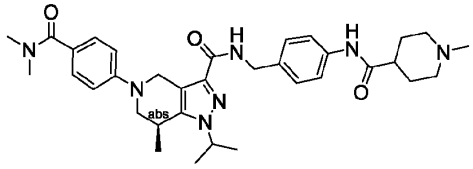
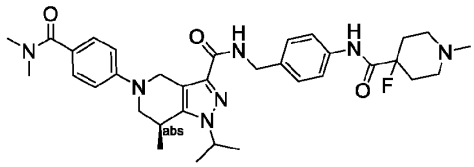
			pyrazolo[4,3-*c*]pyridine-3-carboxamide	
572	Ex. 485		(*S*)-*N*-(4-((*R*)-3-amino-3-methylpyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.4
573	Ex. 485		(*S*)-*N*-(4-((1*RS*,5*SR*)-3,8-diazabicyclo[3.2.1]octane-3-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	631.4

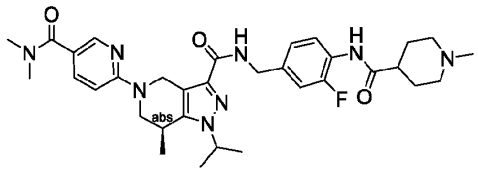
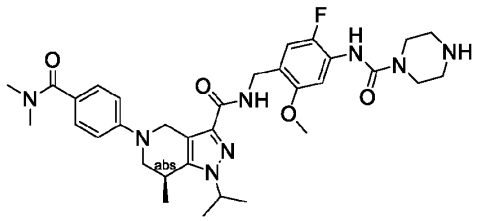
574	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	627.5
575	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*S*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	627.5
576	Ex. 485		(*S*)-*N*-(4-(1,4-diazepane-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-	619.5

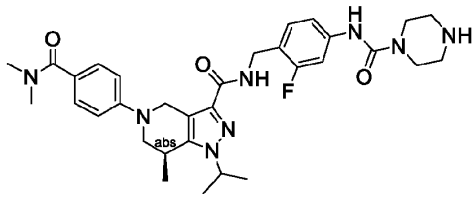
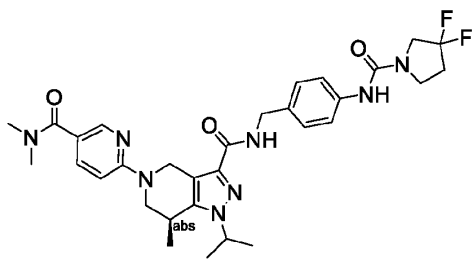
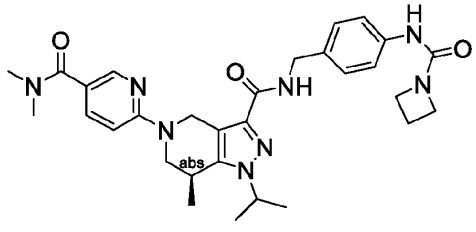
			1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
577	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-((*R*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	631.5
578	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-((*S*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	631.5

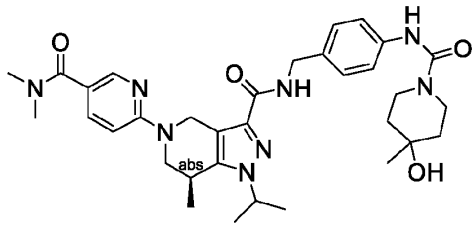
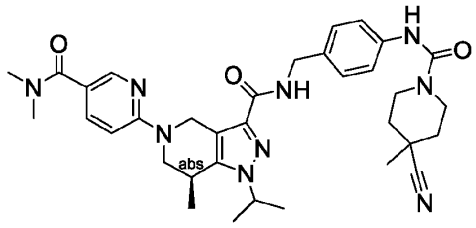
579	Ex. 567		(*S*)-*N*-(4-(3-(2,2-difluoroethyl)ureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	583.4
580	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	619.4
581	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-methyl-3-(methylamino)azetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.4

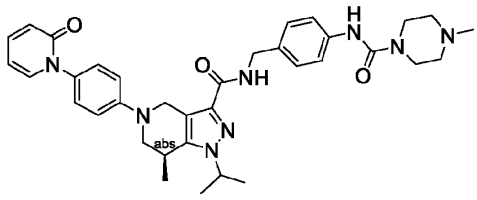
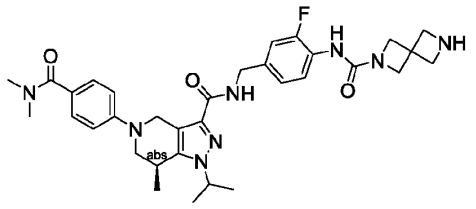
582	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*RS*)-3-methyl-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.4
583	Ex. 485		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.4

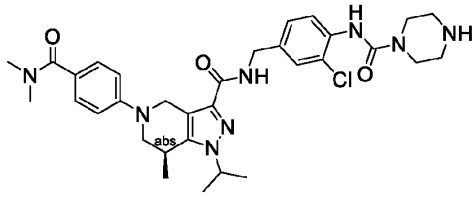
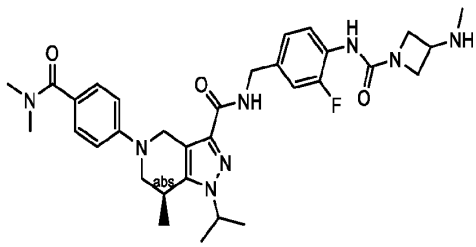
584	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-fluoroazetidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	577.4
585	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methylpiperidine-4-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	600.5
586	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(4-fluoro-1-methylpiperidine-4-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	618.5

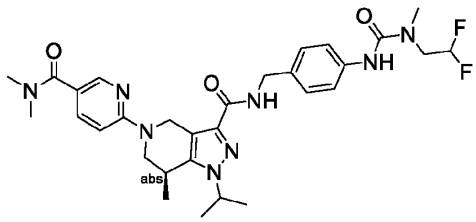
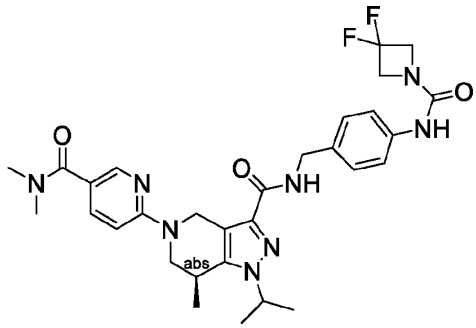
587	Ex. 128[s]		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(1-methylpiperidine-4-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	619.5
588	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(5-fluoro-2-methoxy-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	635.4

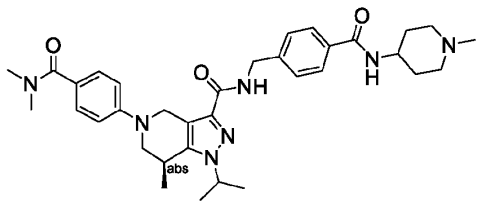
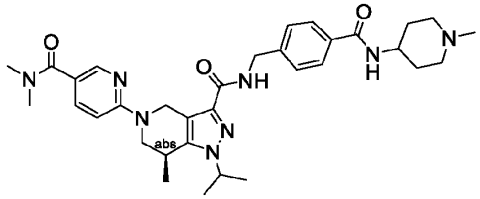
589	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(2-fluoro-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	605.5
590	Ex. 567		(*S*)-*N*-(4-(3,3-difluoropyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	609.5
591	Ex. 567		(*S*)-*N*-(4-(azetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	559.3

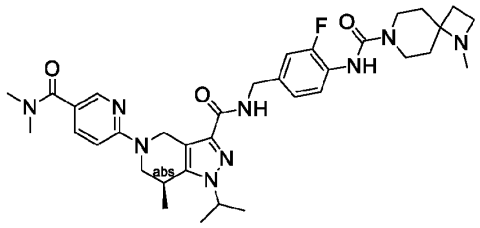
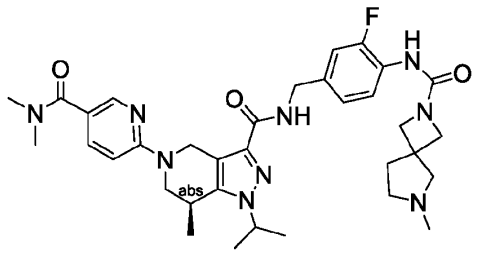
592	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(4-hydroxy-4-methylpiperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	617.4
593	Ex. 567		(*S*)-*N*-(4-(4-cyano-4-methylpiperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	626.5

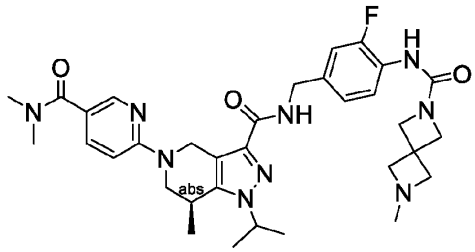
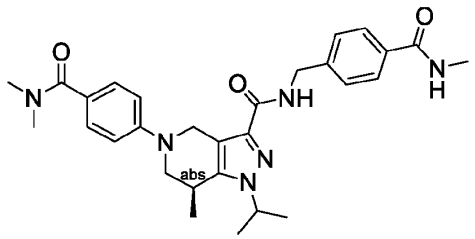
594	Ex. 485		(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(4-(2-oxopyridin-1(2*H*)-yl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	623.5
595	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	617.7

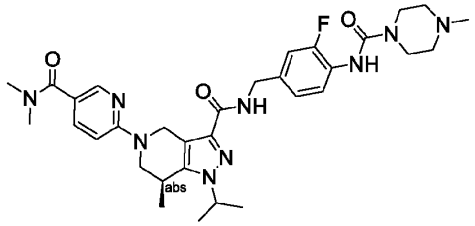
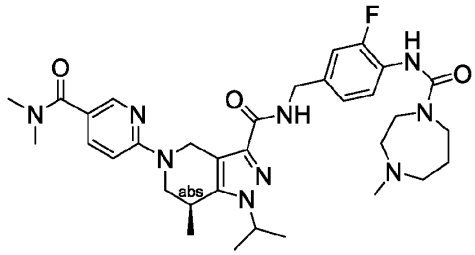
596	Ex. 485		(*S*)-*N*-(3-chloro-4-(piperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	621.3
597	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(3-(methylamino)azetidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	605.6

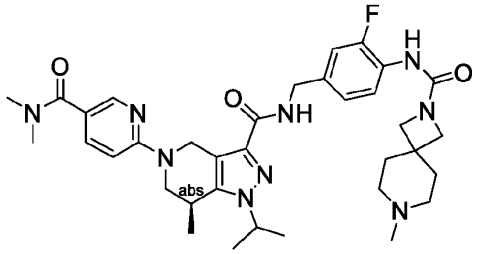
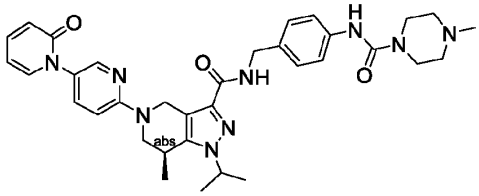
598	Ex. 567		(*S*)-*N*-(4-(3-(2,2-difluoroethyl)-3-methylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	597.5
599	Ex. 567		(*S*)-*N*-(4-(3,3-difluoroazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	595.4

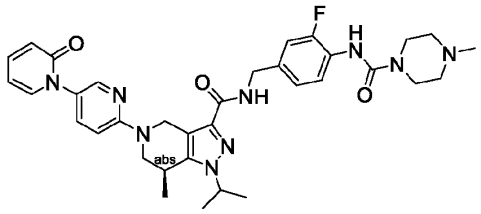
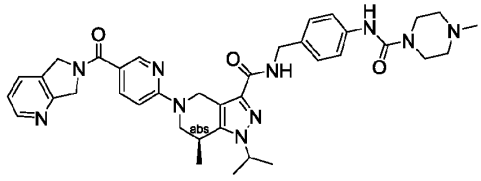
600			(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((1-methylpiperidin-4-yl)carbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	600.5
601	Ex. 132[ora]		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-((1-methylpiperidin-4-yl)carbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.5

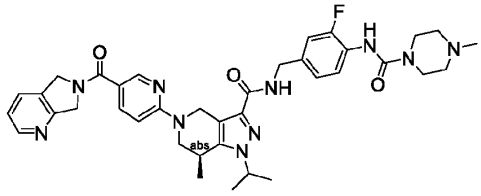
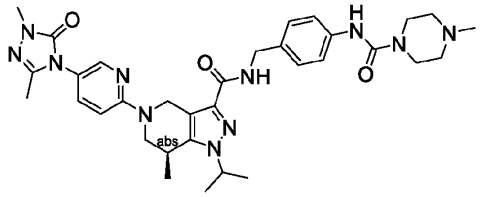
602	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(1-methyl-1,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	660.5
603	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.4]octane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	646.5

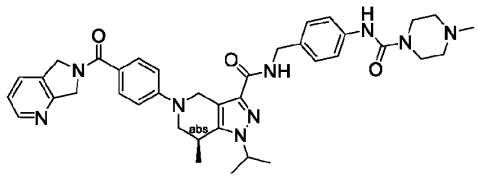
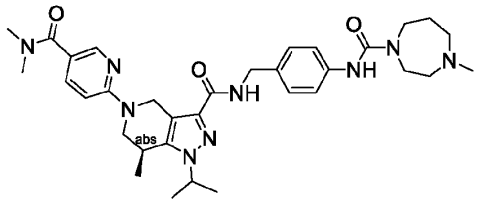
604	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	632.5
605	Ex. 132[o]		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	517.4

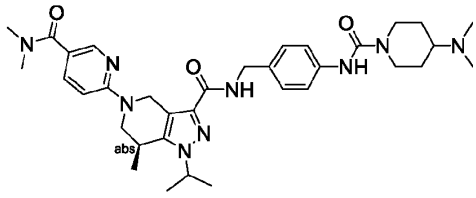
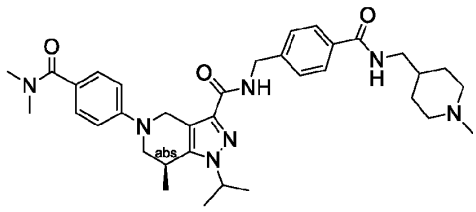
606	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	620.5
607	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	634.5

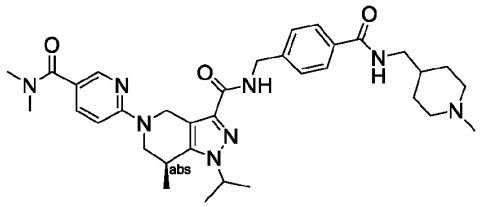
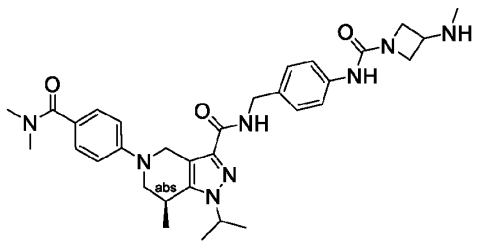
608	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	660.6
609	Ex. 125		(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	624.7

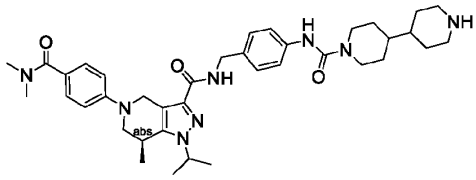
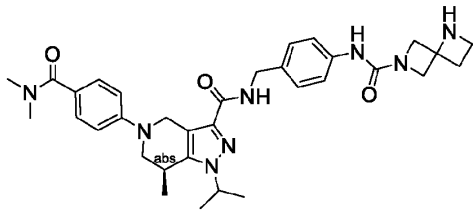
610	Ex. 125		(*S*)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.7
611	Ex. 125		(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	677.5

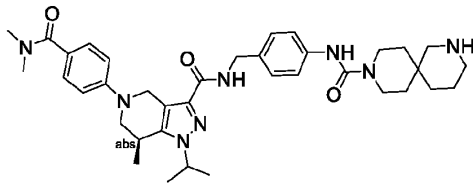
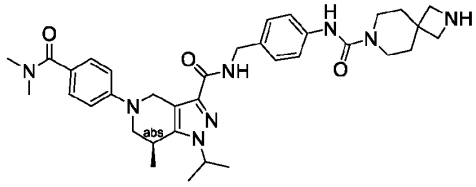
612	Ex. 125		(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	695.5
613	Ex. 127		(*S*)-5-(5-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.5

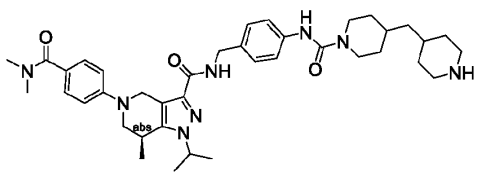
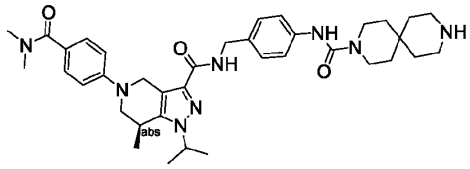
614	Ex. 125[q]		(*S*)-5-(4-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	676.6
615	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.5

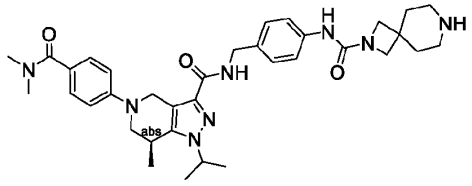
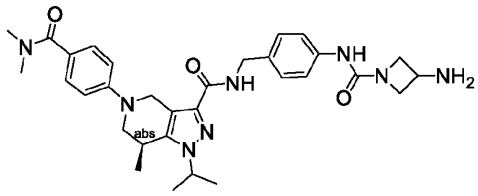
616	Ex. 567		(*S*)-*N*-(4-(4-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	630.5
617	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(((1-methylpiperidin-4-yl)methyl)carbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	614.4

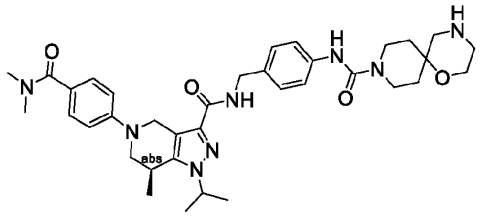
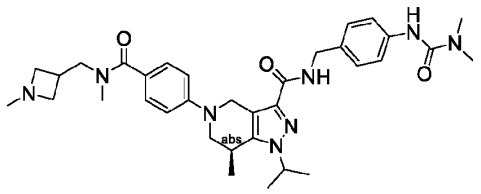
618	Ex. 128		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(((1-methylpiperidin-4-yl)methyl)carbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.4
619	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-(methylamino)azetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.4

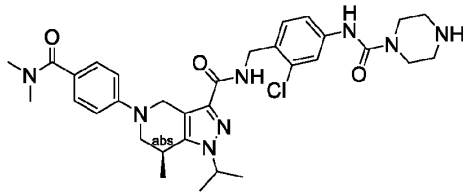
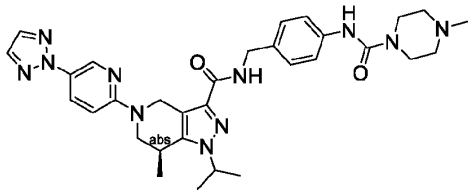
620	Ex. 485		(*S*)-*N*-(4-([4,4'-bipiperidine]-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	669.6
621	Ex. 485		(*S*)-*N*-(4-(1,6-diazaspiro[3.3]heptane-6-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	599.5

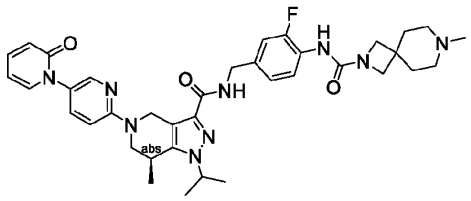
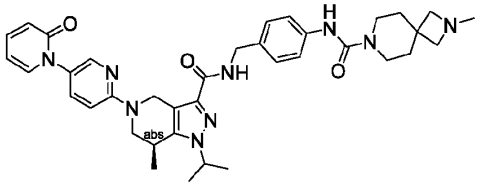
622	Ex. 485		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2,9-diazaspiro[5.5]undecane-9-carboxamide	655.6
623	Ex. 485		(*S*)-*N*-(4-(2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	627.6

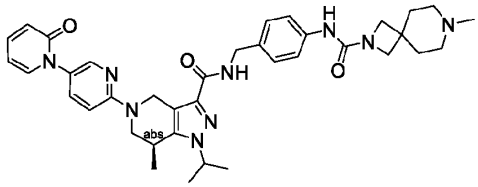
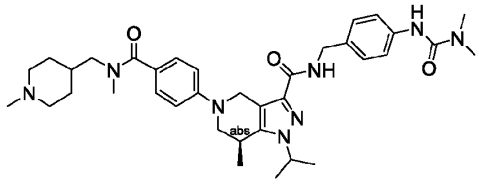
624	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-(piperidin-4-ylmethyl)piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	683.6
625	Ex. 485		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-3,9-diazaspiro[5.5]undecane-3-carboxamide	655.6

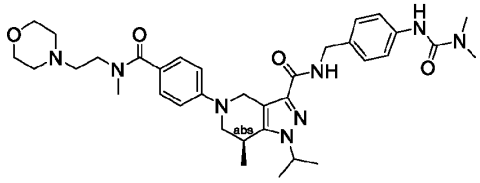
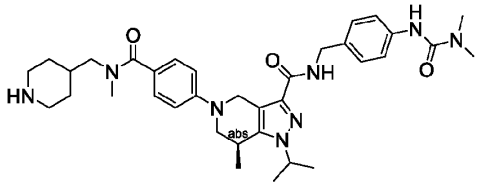
626	Ex. 485		(*S*)-*N*-(4-(2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	627.5
627	Ex. 485		(*S*)-*N*-(4-(3-aminoazetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	573.4

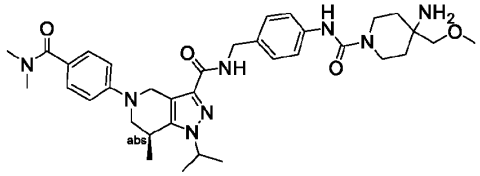
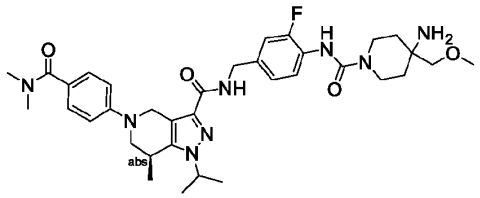
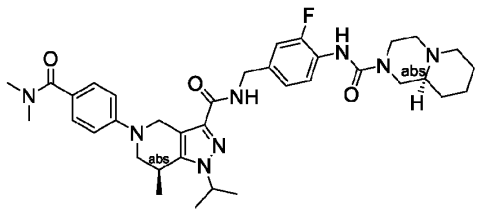
628	Ex. 485		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-1-oxa-4,9-diazaspiro[5.5]undecane-9-carboxamide	657.6
629	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-methylazetidin-3-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.5

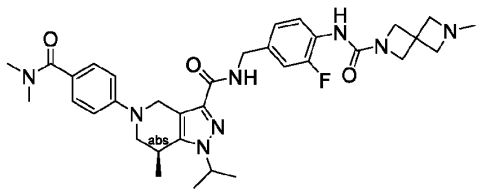
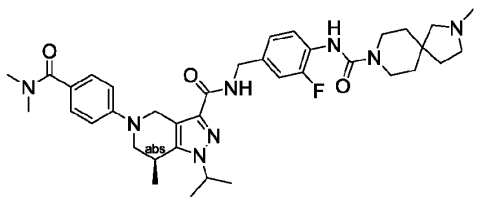
630	Ex. 485		(*S*)-*N*-(2-chloro-4-(piperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	621.4
631	Ex. 125[q]		(*S*)-5-(5-(2*H*-1,2,3-triazol-2-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	598.5

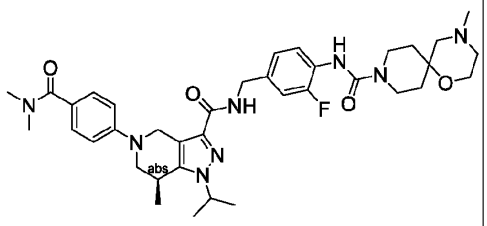
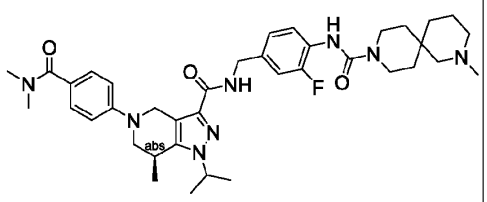
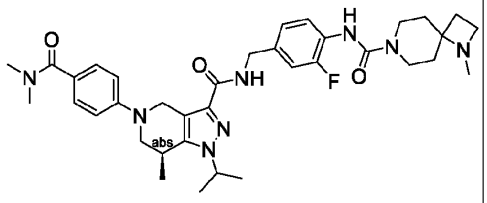
632	Ex. 567		(*S*)-*N*-(3-fluoro-4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	682.6
633	Ex. 567		(*S*)-1-isopropyl-7-methyl-*N*-(4-(2-methyl-2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	664.5

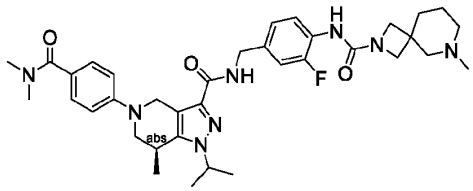
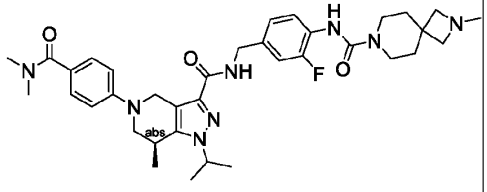
634	Ex. 567		(*S*)-1-isopropyl-7-methyl-*N*-(4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	664.6
635	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-methylpiperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	643.5

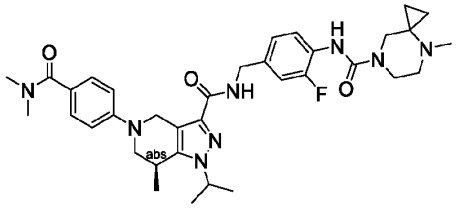
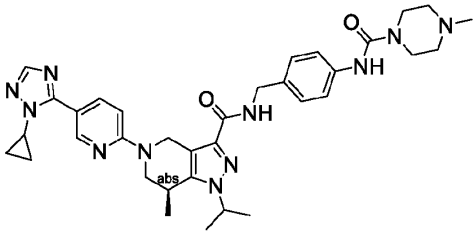
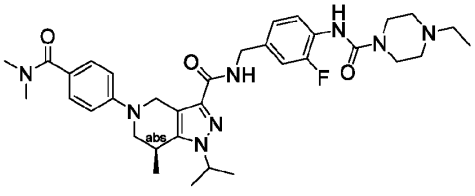
636	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(2-morpholinoethyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	645.5
637	Ex. 395[fop]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(piperidin-4-ylmethyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	629.7

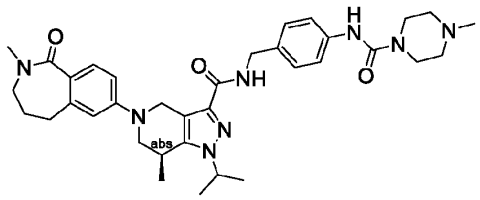
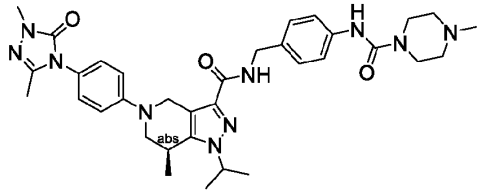
638	Ex. 567		(*S*)-*N*-(4-(4-amino-4-(methoxymethyl)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	645.5
639	Ex. 567		(*S*)-*N*-(4-(4-amino-4-(methoxymethyl)piperidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	663.6
640	Ex. 567		(*S*)-*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamid	659.6

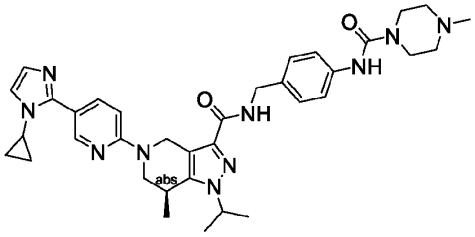
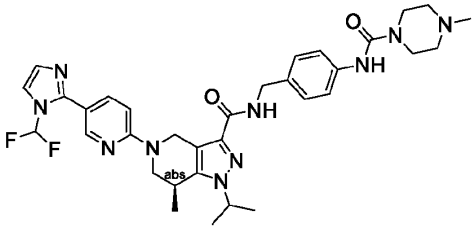
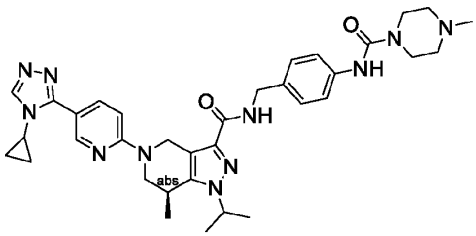
			o)methyl)-2-fluorophenyl)octahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carboxamide	
641	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	631.5
642	Ex. 567		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-2-methyl-2,8-diazaspiro[4.5]decane-8-carboxamide	673.6

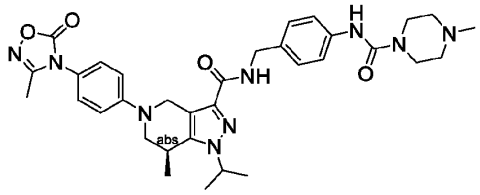
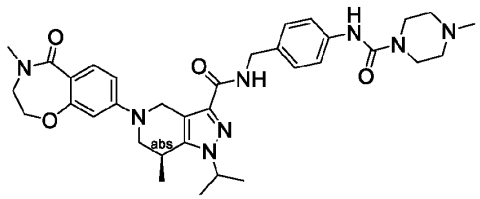
643	Ex. 567		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-4-methyl-1-oxa-4,9-diazaspiro[5.5]undecane-9-carboxamide	689.7
644	Ex. 567		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-2-methyl-2,9-diazaspiro[5.5]undecane-9-carboxamide	687.6
645	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(1-methyl-1,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-1-	659.6

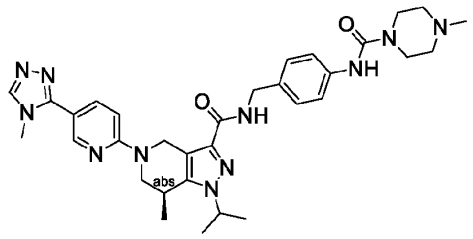
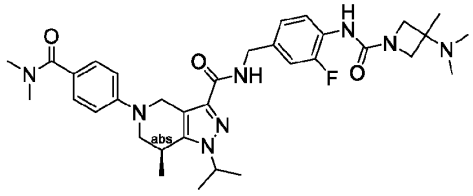
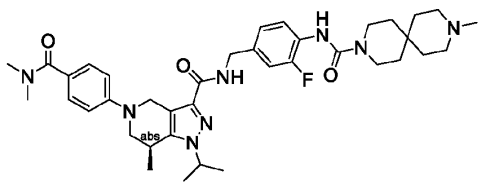
			isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
646	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	659.6
647	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(2-methyl-2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	659.5

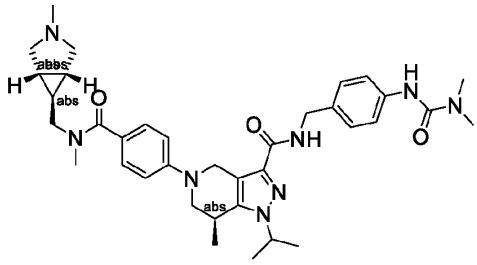
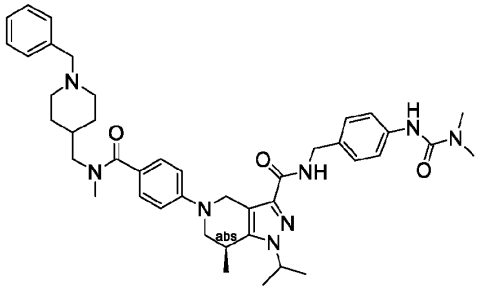
648	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(4-methyl-4,7-diazaspiro[2.5]octane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	645.6
649	Ex. 515[y]		(*S*)-5-(5-(1-cyclopropyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	638.5
650	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(4-ethylpiperazine-1-carboxamido)-3-fluorobenzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3	633.5

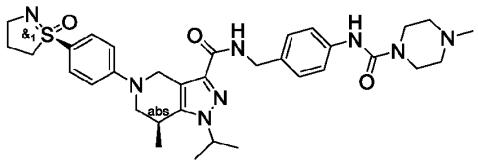
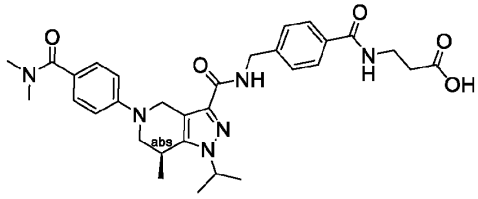
			-*c*]pyridine-3-carboxamide	
651	Ex. 127[i]		(*S*)-1-isopropyl-7-methyl-5-(2-methyl-1-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*c*]azepin-7-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	627.5
652	Ex. 127[i]		(*S*)-5-(4-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	641.3

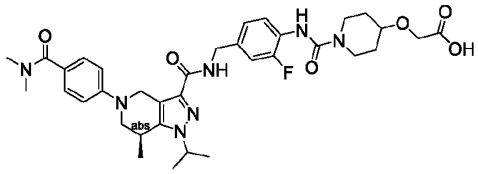
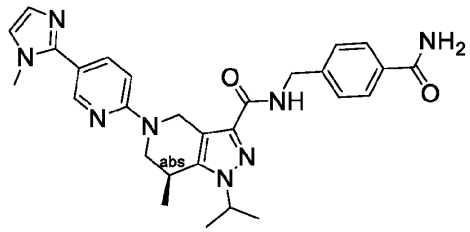
653	Ex. 125^{wx}		(*S*)-5-(5-(1-cyclopropyl-1*H*-imidazol-2-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	637.5
654	Ex. 125^{wx}		(*S*)-5-(5-(1-(difluoromethyl)-1*H*-imidazol-2-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	647.5
655	Ex. 125^{wx}		(*S*)-5-(5-(4-cyclopropyl-4*H*-1,2,4-triazol-3-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-	638.6

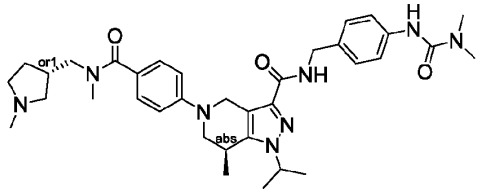
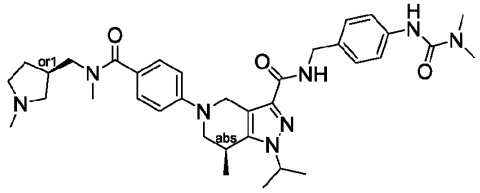
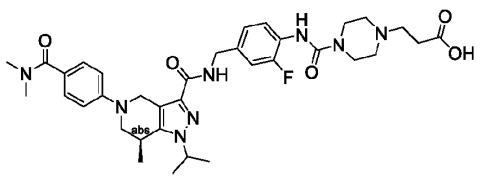
			1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
656	Ex. 127[i]		(*S*)-1-isopropyl-7-methyl-5-(4-(3-methyl-5-oxo-1,2,4-oxadiazol-4(5*H*)-yl)phenyl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	628.5
657	Ex. 127[i]		(*S*)-1-isopropyl-7-methyl-5-(4-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*f*][1,4]oxazepin-8-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	629.4

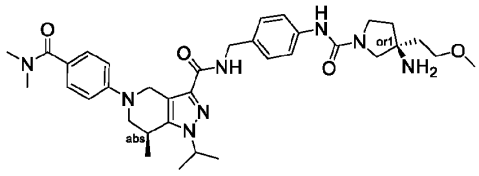
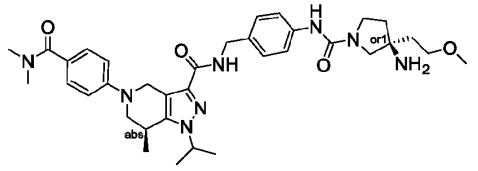
658	Ex. 515[y]		(*S*)-1-isopropyl-7-methyl-5-(5-(4-methyl-4*H*-1,2,4-triazol-3-yl)pyridin-2-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	612.5
659	Ex. 567		(*S*)-*N*-(4-(3-(dimethylamino)-3-methylazetidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.3
660	Ex. 567		*(S)*-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-	687.4

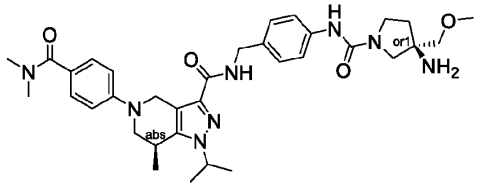
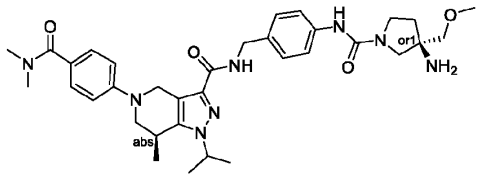
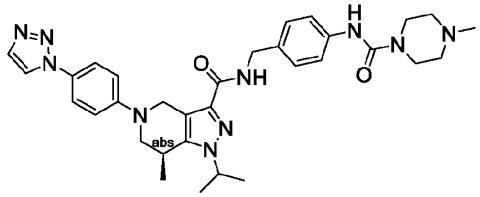
			fluorophenyl)-9-methyl-3,9-diazaspiro[5.5]undecane-3-carboxamide	
661	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(((1*R*,5*S*,6*r*)-3-methyl-3-azabicyclo[3.1.0]hexan-6-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	641.5
662	Ex. 395[fo]		(*S*)-5-(4-(((1-benzylpiperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	720.3

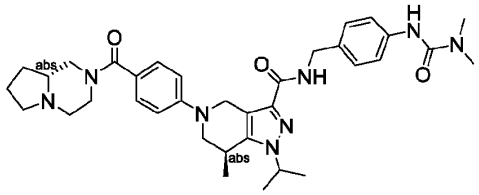
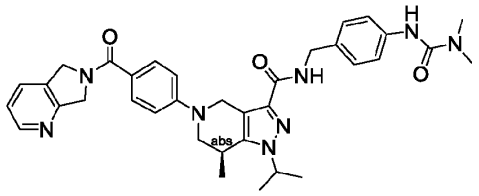
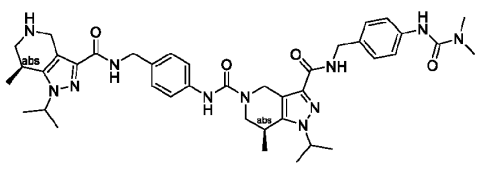
663	Ex. 125[q]		(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(4-((*S*)-1-oxido-4,5-dihydro-3*H*-1l6-isothiazol-1-yl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.3
664	Ex. 132[or]		(*S*)-3-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)benzamido)propanoic acid	575.4

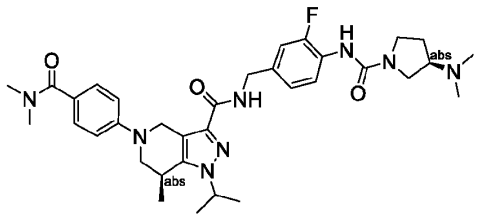
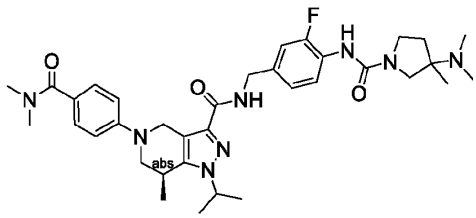
665	Ex. 567		(*S*)-2-((1-((4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)carbamoyl)piperidin-4-yl)oxy)acetic acid	678.5
666	Ex. 127[i]		(*S*)-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	513.3

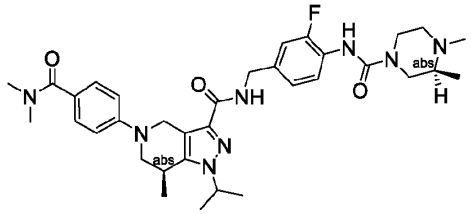
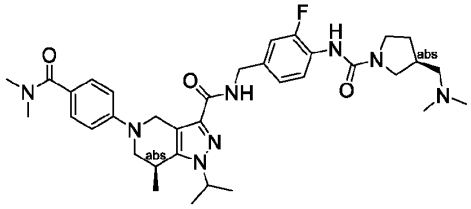
667 ^	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(((*R**)-1-methylpyrrolidin-3-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	629.5
668 ^	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(((*R**)-1-methylpyrrolidin-3-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	629.5
669	Ex. 567		(*S*)-3-(4-((4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-	677.5

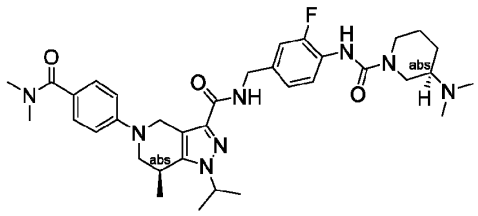
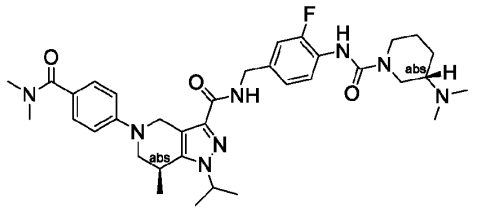
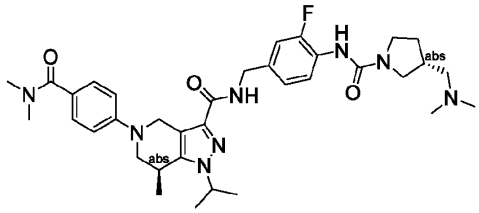
			fluorophenyl)carbamoyl)piperazin-1-yl)propanoic acid	
670 ^	Ex. 567		(*S*)-*N*-(4-((*R**)-3-amino-3-(2-methoxyethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	645.3
671 ^	Ex. 567		(*S*)-*N*-(4-((*R**)-3-amino-3-(2-methoxyethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	645.4

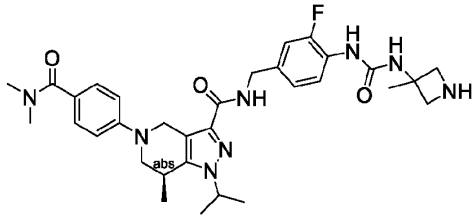
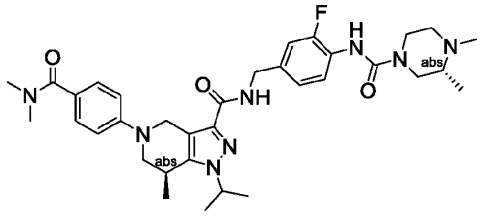
672 ^	Ex. 567		(*S*)-*N*-(4-((*R**)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	631.3
673 ^	Ex. 567		(*S*)-*N*-(4-((*R**)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	631.3
674	Ex. 127[q]		(*S*)-5-(4-(1*H*-1,2,3-triazol-1-yl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-	597.4

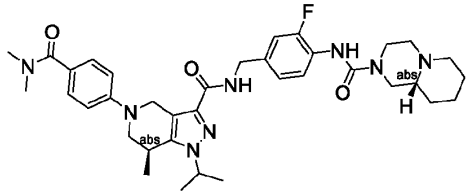
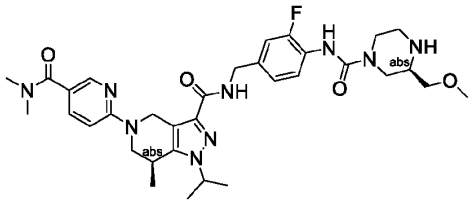
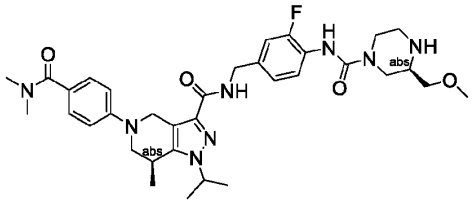
			1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
675	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carbonyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	627.6
676	Ex. 193[fo]		(*S*)-5-(4-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	621.5
677			(*S*)-N^3-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-N^5-(4-(((*S*)-1-isopropyl-7-methyl-	752.4

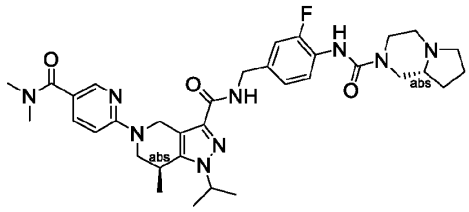
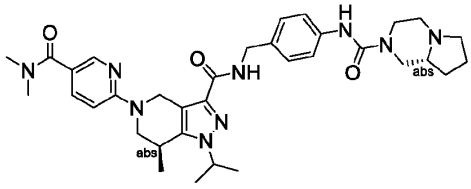
			4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridine-3,5-dicarboxamide	
678	Ex. 567		(*S*)-*N*-(4-((*R*)-3-(dimethylamino)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.4
679	Ex. 567		(7*S*)-*N*-(4-(3-(dimethylamino)-3-methylpyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-	647.6

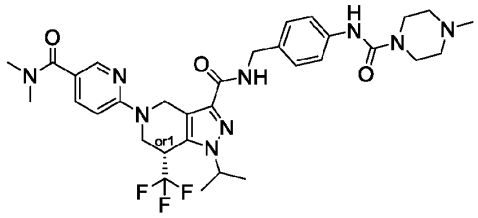
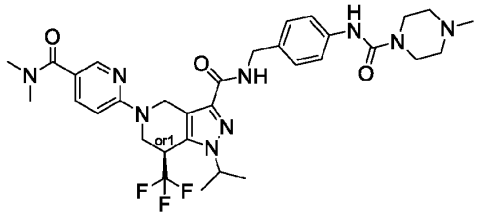
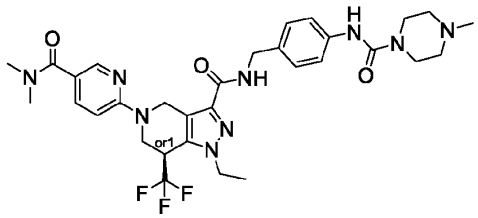
			1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
680	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*S*)-3,4-dimethylpiperazine-1-carboxamido)-3-fluorobenzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.6
681	Ex. 567		(*S*)-*N*-(4-((*S*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	647.6

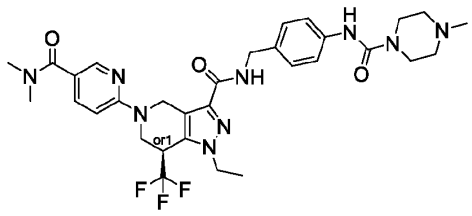
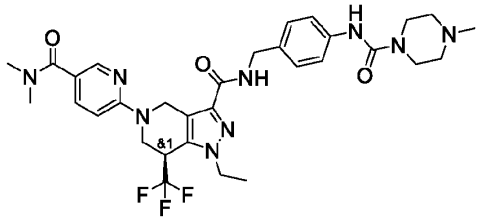
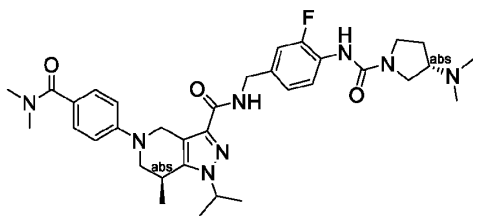
682	Ex. 567		(*S*)-*N*-(4-((*R*)-3-(dimethylamino)piperidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	647.6
683	Ex. 567		(*S*)-*N*-(4-((*S*)-3-(dimethylamino)piperidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	647.6
684	Ex. 567		(*S*)-*N*-(4-((*R*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-	647.6

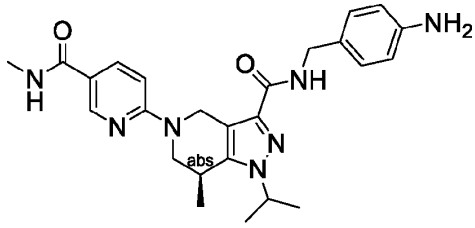
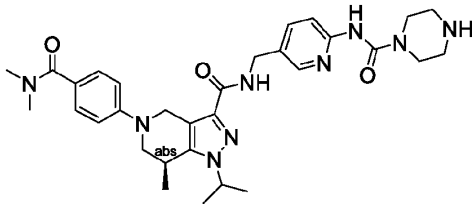
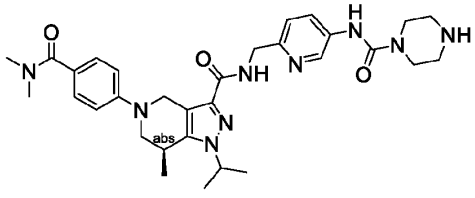
			isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
685	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(3-(3-methylazetidin-3-yl)ureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	605.5
686	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*R*)-3,4-dimethylpiperazine-1-carboxamido)-3-fluorobenzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	633.6

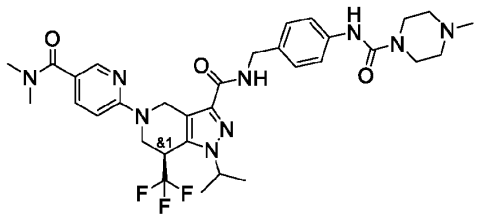
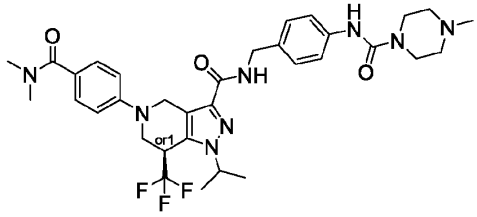
687	Ex. 567		(*R*)-*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)octahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carboxamide	659.6
688	Ex. 485		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-((*R*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	650.7
689	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-((*R*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-	649.5

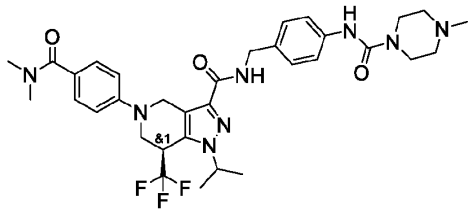
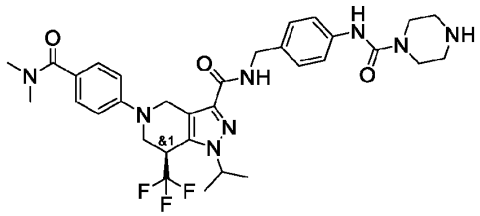
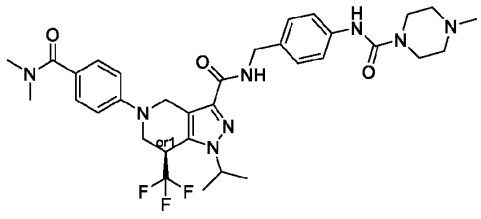
			4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
690	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	646.6
691	Ex. 567		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	628.5

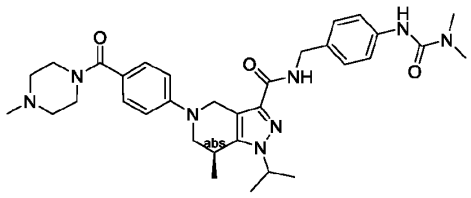
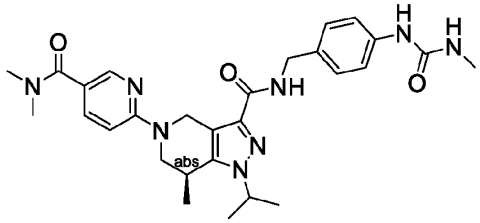
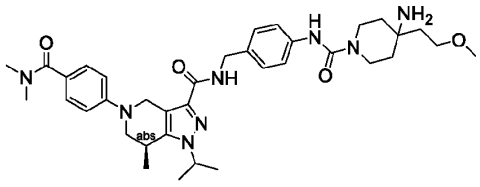
692 ^	Ex. 546[a]		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	656.4
693 ^	Ex. 546[a]		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	656.4
694 ^	Ex. 4[i]		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-	642.3

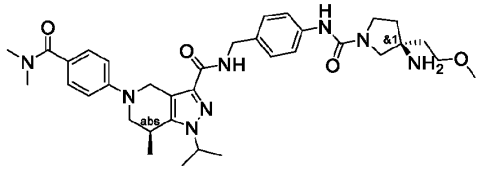
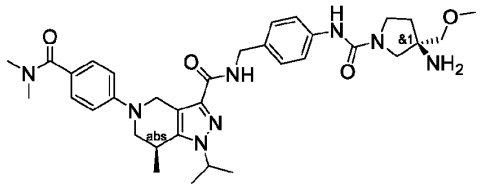
			3-carboxamide	
695^	Ex. 4[i]		*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.3
696	Ex. 4[i]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	642.4
697	Ex. 567		(*S*)-*N*-(4-((*S*)-3-(dimethylamino)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcar	633.5

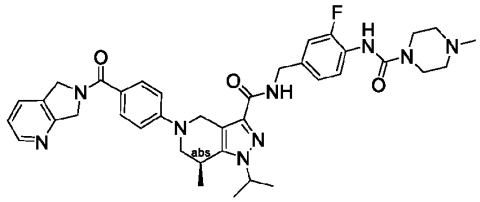
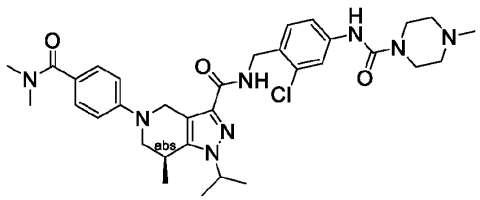
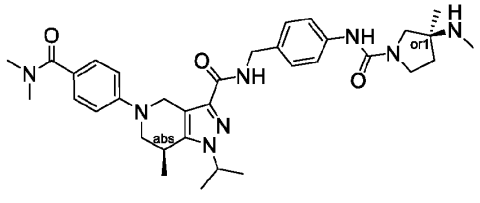
			bamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
698	Ex. 128		(*S*)-*N*-(4-aminobenzyl)-1-isopropyl-7-methyl-5-(5-(methylcarbamoyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	462.4
699	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-((6-(piperazine-1-carboxamido)pyridin-3-yl)methyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	588.4
700	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-((5-(piperazine-1-	588.4

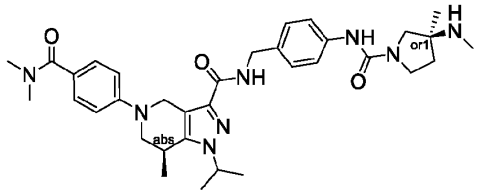
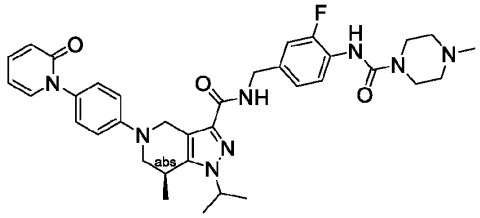
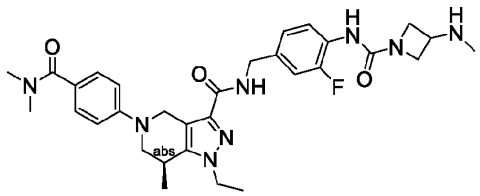
			carboxamido)pyridin-2-yl)methyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
701	Ex. 546[i]		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	656.4
702^	Ex. 4[i]		*rel*-(*R* or *S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	655.3

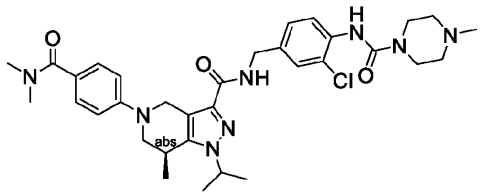
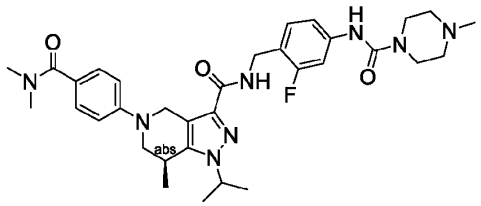
703	Ex. 4[i]		*rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	655.3
704	Ex. 485		*rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(piperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	641.4
705 ^	Ex. 4[i]		*rel*-(*R* or *S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-	655.3

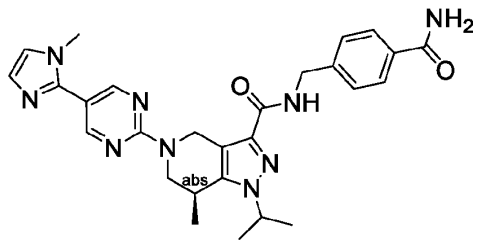
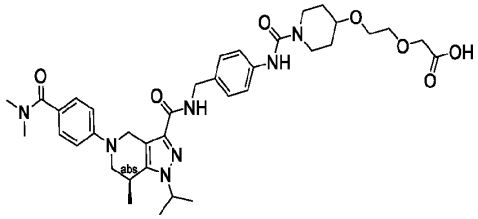
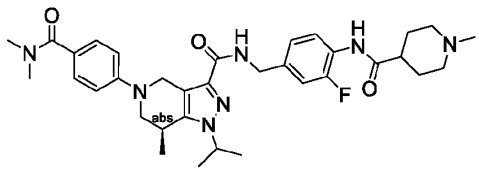
			carboxamide	
706	Ex. 395[fo]		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(4-methylpiperazine-1-carbonyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.5
707	Ex. 128		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	533.4
708	Ex. 567		(*S*)-*N*-(4-(4-amino-4-(2-methoxyethyl)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-	659.5

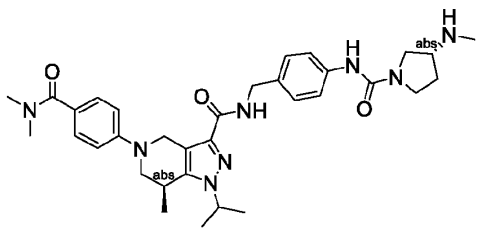
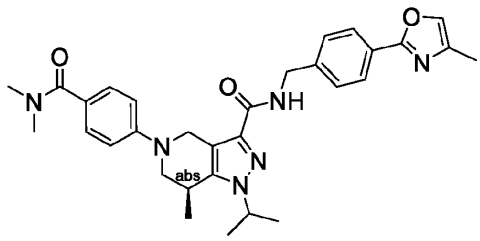
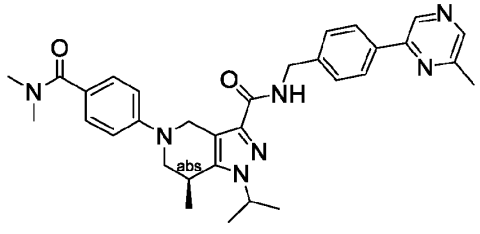
			4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
709	Ex. 567		(*S*)-*N*-(4-((*RS*)-3-amino-3-(2-methoxyethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	645.5
710	Ex. 567		(*S*)-*N*-(4-((*RS*)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	631.5

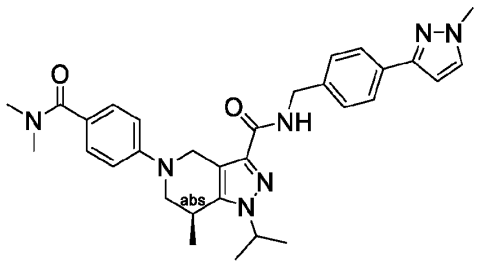
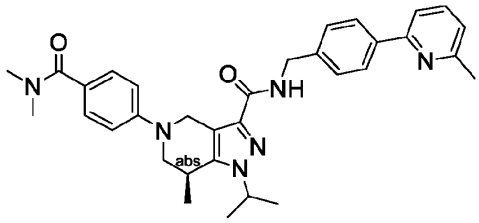
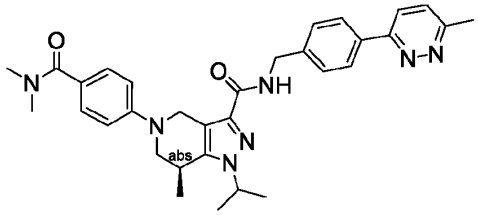
711	Ex. 125[q]		(*S*)-5-(4-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)phenyl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	694.5
712	Ex. 567		(*S*)-*N*-(2-chloro-4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	635.4
713 ^	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R**)-3-methyl-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-	615.4

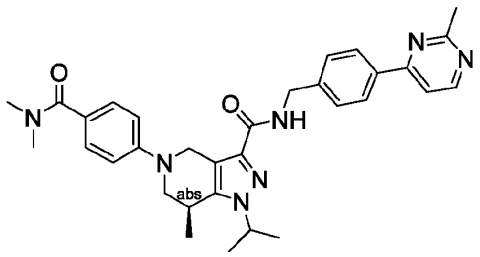
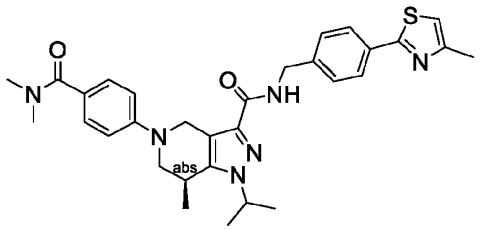
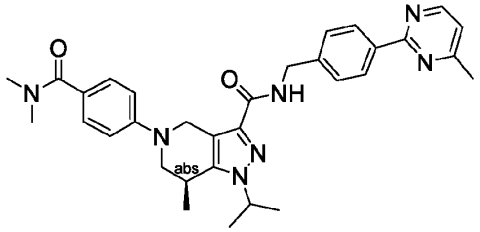
			1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
714^	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R**)-3-methyl-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	616.3
715	Ex. 128		(*S*)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-5-(4-(2-oxopyridin-1(2*H*)-yl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	641.7
716	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-ethyl-*N*-(3-fluoro-4-(3-(methylamino)azetidine-	591.5

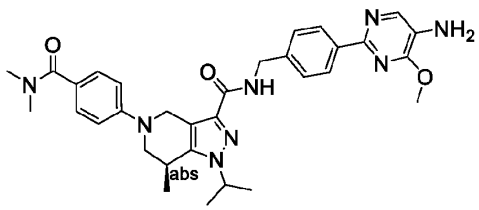
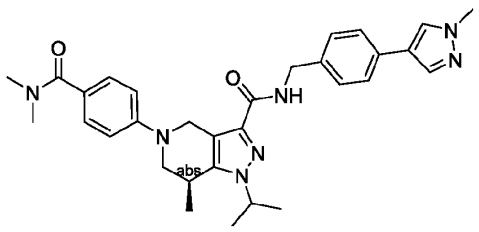
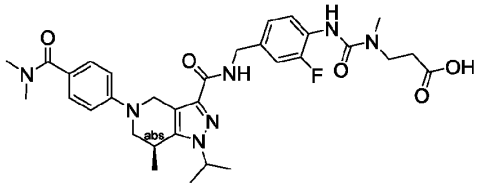
			1-carboxamido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
717	Ex. 567		(*S*)-*N*-(3-chloro-4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	635.3
718	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(2-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	619.5

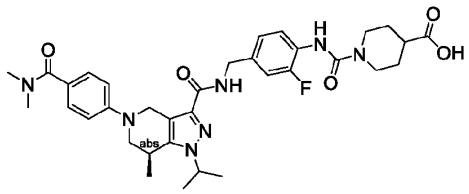
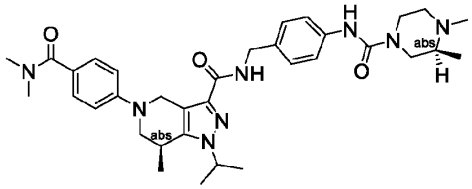
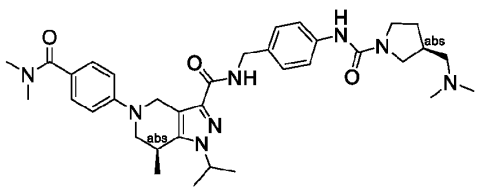
719	Ex. 127		(*S*)-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	514.3
720	Ex. 485		(*S*)-2-(2-((1-((4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamoyl)piperidin-4-yl)oxy)ethoxy)acetic acid	704.4
721			(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(1-methylpiperidine-4-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	618.5

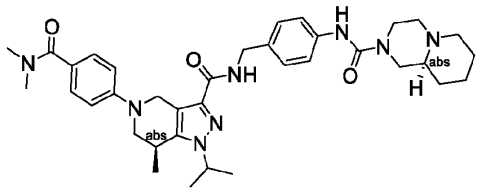
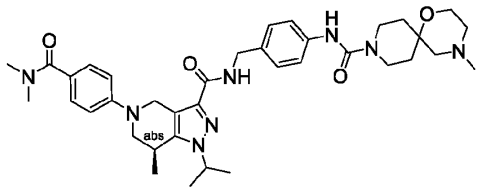
722	Ex. 485		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R*)-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.4
723	Ex. 132[otu]		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methyloxazol-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	541.3
724	Ex. 132[otu]		(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methylpyrazin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	552.5

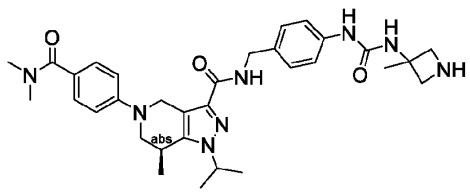
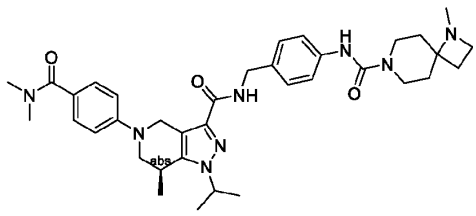
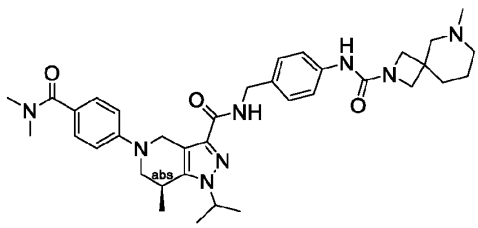
725	Ex. 132[otu]		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methyl-1*H*-pyrazol-3-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	540.4
726	Ex. 132[otu]		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methylpyridin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	551.3
727	Ex. 132[otu]		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methylpyridazin-3-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	552.3

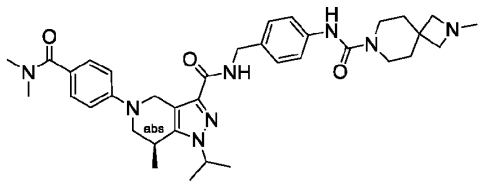
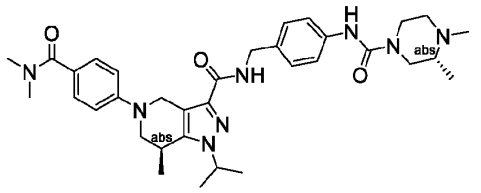
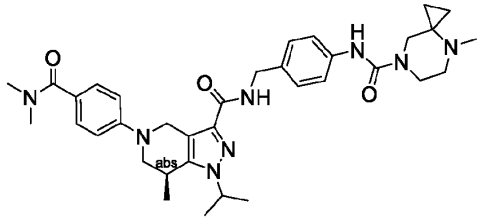
728	Ex. 132^{otu}		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(2-methylpyrimidin-4-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	552.5
729	Ex. 132^{otu}		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylthiazol-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	557.4
730	Ex. 132^{otu}		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	552.4

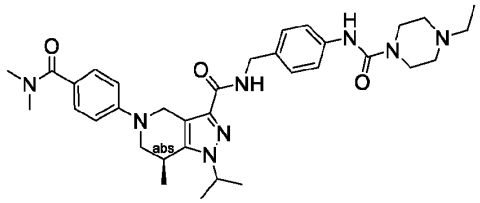
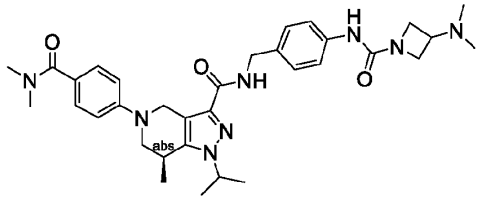
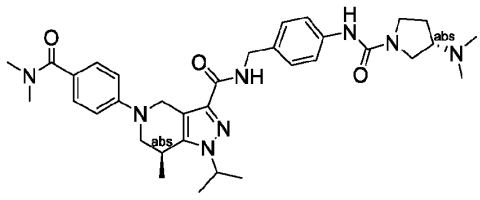
731	Ex. 132[otu]		(*S*)-*N*-(4-(5-amino-4-methoxypyrimidin-2-yl)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	583.5
732	Ex. 132[otu]		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methyl-1*H*-pyrazol-4-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	540.5
733	Ex. 567		(*S*)-3-(3-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-1-methylureido)propanoic acid	622.5

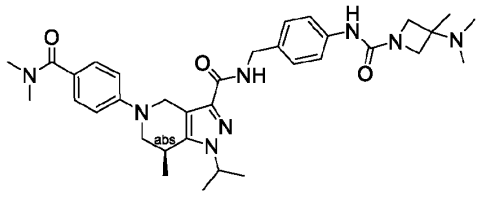
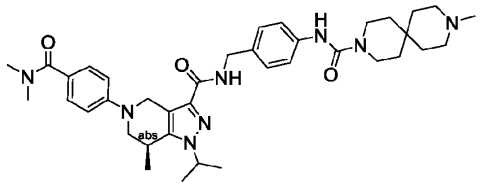
734	Ex. 567		(*S*)-1-((4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)carbamoyl)piperidine-4-carboxylic acid	648.5
735	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*S*)-3,4-dimethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.5
736	Ex. 567		(*S*)-*N*-(4-((*S*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3	629.5

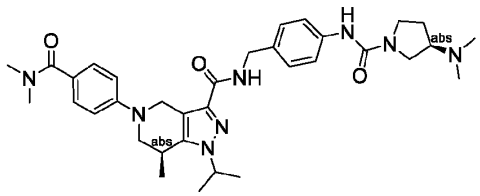
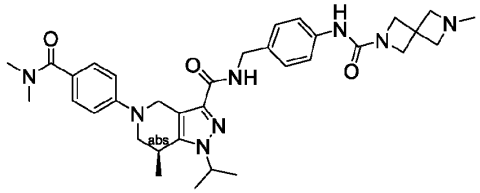
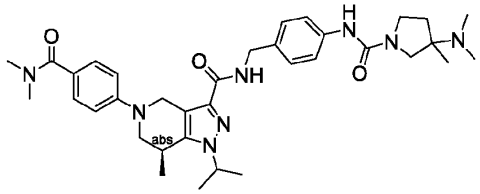
			-*c*]pyridine-3-carboxamide	
737	Ex. 567		(*S*)-*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)octahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carboxamide	641.5
738	Ex. 567		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-4-methyl-1-oxa-4,9-diazaspiro[5.5]undecane-9-carboxamide	671.5

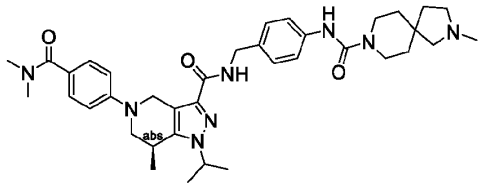
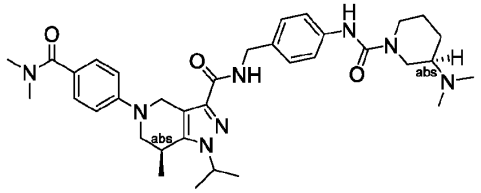
739	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-(3-methylazetidin-3-yl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	587.4
740	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methyl-1,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	641.5
741	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methyl-2,6-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3	641.5

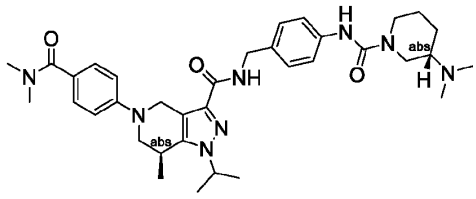
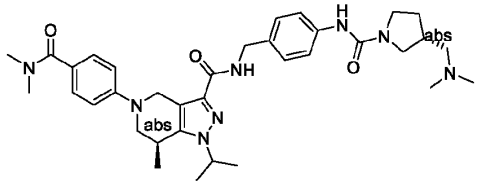
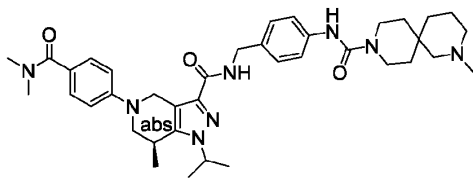
			-*c*]pyridine-3-carboxamide	
742	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(2-methyl-2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	641.5
743	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*R*)-3,4-dimethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.5
744	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-4,7-diazaspiro[2	627.5

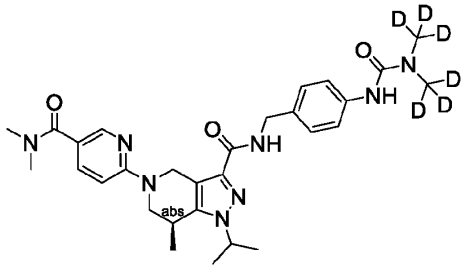
			.5]octane-7-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
745	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(4-ethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.5
746	Ex. 567		(*S*)-*N*-(4-(3-(dimethylamino)azetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	601.5
747	Ex. 567		(*S*)-*N*-(4-((*S*)-3-(dimethylamino)pyrrolidine-1-carboxamido)benzyl)-5-(4-	615.5

			(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
748	Ex. 567		(*S*)-*N*-(4-(3-(dimethylamino)-3-methylazetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.5
749	Ex. 567		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-9-methyl-3,9-diazaspiro[5.5]undecane-3-carboxamide	669.6

750	Ex. 567		(*S*)-*N*-(4-((*R*)-3-(dimethylamino)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	615.6
751	Ex. 567		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methyl-2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	613.5
752	Ex. 567		(7*S*)-*N*-(4-(3-(dimethylamino)-3-methylpyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-	629.5

			tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	
753	Ex. 567		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-methyl-2,8-diazaspiro[4.5]decane-8-carboxamide	655.5
754	Ex. 567		(*S*)-*N*-(4-((*R*)-3-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	629.5

755	Ex. 567		(*S*)-*N*-(4-((*S*)-3-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	629.5
756	Ex. 567		(*S*)-*N*-(4-((*R*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	629.5
757	Ex. 567		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamid	669.5

			o)methyl)phenyl)-2-methyl-2,9-diazaspiro[5.5]undecane-9-carboxamide	
758	Ex. 567		(*S*)-*N*-(4-(3,3-bis(methyl-d_3)ureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide	553.6

^{1}H NMR*= analytical data was obtained as the hydrochloride, trifluoroacetate or formate salt form; Example #^= chiral purification data listed below

[a]: Amide coupling altered: At 0 °C under nitrogen gas, to a stirred solution of amine (1.00 equivalent), acid (1.00 equivalent), HATU (1.05 equivalents) in DMF (0.2 M) was added DIEA (4.50 equivalents). The reaction mixture was stirred at room temperature for 2 h then purified by reverse phase HPLC and lyophilized to give the desired target.

[b]: SNAr altered: A reaction mixture of amine (1.0 equivalent), fluoro-substituted heterocycle (1.3 equivalents), K_2CO_3 (3.0 equivalents) in DMF (0.15M) was stirred at 130 °C for 21 h. The suspension was concentrated *in vacuo* then purified by column chromatography (silica gel, 0-40% EtOAc: PE) to give the desired target.

[c]: Copper(I)-catalyzed cross coupling altered: To 6,7-membered ring lactams (2.0 equivalents) was added a solution of iodo-substituted heterocycle (1.0 equivalents) in dioxane (0.1M) followed by CuI (0.1 equivalent), DMEDA (0.2 equivalent), then Cs_2CO_3 (3.0 equivalents) under nitrogen gas. The reaction mixture was stirred at 120 °C for 16 h then concentrated *in vacuo*. The residue was purified by preparative TLC to give the desired target.

[d]: Amide Coupling altered: To a stirred solution of acid (1.0 equivalent), amine (1.2 equivalent), EDCI (1.4 equivalents), HOBt (1.2 equivalents) in ACN (0.13 M) was added DIEA (3.0 equivalents). The reaction mixture was stirred at room temperature for ~24 h then diluted with H_2O and NH_4Cl (50 mL). The suspension was extracted with DCM (2 x 50 mL). The combined organic layer was concentrated *in vacuo* to give the desired target.

[e]: SNAr altered: A reaction mixture of amine (1.0 equivalent) and fluoro-substituted heterocycle (2.0 equivalents) in H_2O (0.56M) was added DIEA (0.47 mL). The reaction mixture was stirred at 100 °C for 24 h then cooled to room temperature and stirred at room temperature for 72 h. The suspension was quenched with 1M citric acid to pH=3 then extracted with DCM (3x). The organic layers were combined then dried with Na_2SO_4 and concentrated *in vacuo* to give the desired target.

[f]: Palladium coupling altered: A reaction mixture of amine (1.00 equivalent), chloro-substituted heterocycle (3.45 equivalents) and K_3PO_4 (3.00 equivalents) in tert-amyl alcohol (0.1 M) was degassed with nitrogen gas for 5 min before RuPhos Pd G4 (0.100 equivalent) was added. The suspension was degassed with nitrogen gas again for 5 min then stirred at 100 °C for 17 h. The reaction mixture was concentrated via nitrogen gas then dissolved in MeOH and filtered. The filtrate was diluted with EtOAc and filtered through Celite. The filter cake was rinsed with EtOAc. The filtrate was concentrated *in vacuo*. The residue was dissolved in EtOAc and heptane then concentrated *in vacuo* (2x). The residue was dissolved in minimal $CHCl_3$ and purified by column chromatography (silica gel, 0-100% EtOAc: heptane) to give the desired target.

[g]: Palladium coupling altered: To a reaction mixture of amine (1.00 equivalent), chloro-substituted heterocycle (1.20 equivalents) and Cs_2CO_3 (3.00 equivalents) in toluene (0.06 M) was added BINAP (0.10 equivalent) and $Pd_2(dba)_3$ (0.05 equivalent) under nitrogen gas. The reaction mixture was stirred at 110 °C for 16 h then filtered. The filter cake was washed with THF (10 mL) and DCM (10 mL). The filtrate was concentrated *in vacuo* then purified by column chromatography (silica gel, 0:0:100 to 10:90:0 of MeOH: EtOAc: PE) to give the desired target.

[h]: Palladium coupling altered: To a reaction mixture of chloro-substituted heterocycle (1.1 equivalents), amine (1.0 equivalent), K_3PO_4 (3.0 equivalents) and 4Me*t*BuXPhos Pd G3 (0.10 equivalent) under nitrogen was added *tert*-amyl alcohol (0.3 M). The suspension was stirred at 90 °C for 3 h then concentrated *in vacuo*. The residue was dissolved in DCM then filtered. The filtrate was purified by column chromatography (silica gel, 0-10% MeOH: DCM) to give the desired target.

[i]: Palladium Coupling altered: A reaction mixture of amine (1.00 equivalent), chloro-substituted heterocycle (1.25 equivalents) and K_3PO_4 (3.00 equivalents) in *tert*-amyl alcohol (0.1 M) was degassed with nitrogen gas for 5 min before RuPhos Pd G3 (0.102 equivalent) was added. The suspension was degassed with nitrogen gas again for 5 min then stirred at 100 °C for 20 h and at room temperature for ~72 h. The reaction mixture was concentrated via nitrogen gas then dissolved in MeOH and filtered. The filtrate was poured into stirring H_2O and diluted with EtOAc. The aqueous layer was back-extracted with EtOAc (2 x 7 mL). The combined organic layer was washed with brine and dried with Na_2SO_4. The suspension was filtered, concentrated *in vacuo* and dissolved in DCM and minimal $CHCl_3$. The solution was purified by column chromatography (silica gel, 0-100% EtOAc: heptane) to give the desired target.

[i]: SNAr altered: A reaction mixture of amine (1.0 equivalent), fluoro-substituted heterocycle (1.2 equivalents) and CsF (5.0 equivalents) in DMSO (0.1 M) was stirred at 130 °C for 48 h then an additional portion of fluoro-substituted heterocycle (2.4 equivalents) was added. The reaction mixture was stirred at 130 °C for 24 h then lyophilized to give the desired target.

[k]: SNAr altered: To a solution of amine (1.0 equivalent) in *n*-butyl acetate (0.3 M) was added chloro-substituted heterocycle (1.2 equivalents) and K_3PO_4 (3.0 equivalents). The reaction mixture was stirred at 115 °C for 2 h then diluted with ACN and filtered. The filtrate was concentrated *in vacuo* to give the desired target.

[l]: Palladium Coupling altered: A reaction mixture of amine (1.00 equivalent), chloro-substituted heterocycle (1.40 equivalents), K_3PO_4 (3.00 equivalents) and RuPhos Pd G3 (0.08 equivalent) were degassed with nitrogen gas then *tert*-amyl alcohol (0.3 M) was added. The suspension was stirred at 90 °C for 2 h then 4Me*t*BuXPhos Pd G3 (0.10 equivalent). The reaction mixture was stirred at 90 °C for 1 h then concentrated *in vacuo*. The residue was dissolved in DCM and filtered. The filtrate was purified by column chromatography (silica gel, 0-10% MeOH: DCM) to give the desired target. [m]: Addition of deprotection after the SNAr: At 0 °C under nitrogen gas, to a solution of ether (1.0 equivalent) in DCM (0.2 M) was added 2M BBr_3 in DCM (2.0 equivalents) then stirred at room temperature for 16 h. At 0 °C, an additional portion of 2M BBr_3 in DCM (1.4 equivalents) was added. The reaction mixture was stirred at room temperature for 16 h. The suspension was quenched with H_2O (4 mL) at 0 °C then basified with 15% aqueous NaOH to pH~8. The basic mixture was extracted with EtOAc (4 x 20 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the desired target.

[n]: Addition of methylation after the lactam cyclization: To a reaction mixture of lactam (1.0 equivalent) in ACN (0.1 M) and DMF (0.1 M) was added Cs_2CO_3 (3.0 equivalents). The suspension was stirred at 60 °C for 1 h then MeI (13.0 equivalents) was added. The reaction mixture was stirred at 60 °C for 16 h then concentrated *in vacuo*. The residue was purified by reverse phase HPLC (C_{18} 150 mm x 30 mm x 5 µm column, Mobile Phase A: H_2O (0.05% formic acid)/Mobile Phase B: ACN, 21 to 61% of Mobile Phase B over 9 min then held at 100% of Mobile Phase B for 2 min; flow rate= 30 mL/min) to give the desired target.

[o]: Amide Coupling altered: A reaction mixture of acid (1.0 equivalent), amine (1.3 equivalent), EDCI (1.5 equivalents), HOPO (1.2 equivalents) and TEA (4.0 equivalents) in ACN (0.08 M) were stirred at room temperature for ~24 h then diluted with H_2O (2 mL). The suspension was extracted with DCM (3 x 2 mL). The combined organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. The residue was suspended in DMSO then filtered and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 25 to 95% of Mobile Phase B over 10.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide to give the desired target.

[p]: Addition of deprotection in final step: A reaction solution of BOC-protected amine (1.0 equivalent) in DCM (0.07 M) was added TFA (0.3 M). The suspension was stirred at room temperature for 20 min then concentrated *in vacuo*. The residue was dissolved in DMSO then filtered and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 60 to 80% of Mobile Phase B over 10.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide to give the desired target.

[q]: Palladium Coupling altered: Under nitrogen gas, a reaction mixture of acid (1.0 equivalent), bromo-substituted heterocycle (1.1 equivalents), potassium trimethylsilanolate (3.2 equivalents) and P(*t*-Bu)$_3$ Pd G2 (0.1 equivalent) in *tert*-amyl alcohol (0.05 M). The suspension was degassed for 5 min then stirred at 60 °C for 90 min then phosphoric acid (4.0 equivalents) was added. The reaction mixture was diluted with H_2O (3 mL) to pH= 3 then extracted with EtOAc (2 x 3 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was suspended in heptane, sonicated then filtered. The filter cake was washed with heptane then dried further under high vacuo. The solid was collected to provide to give the desired target.

[r]: Addition of hydrolysis in last step: To an ester (1.0 equivalent) in ACN (0.03 M) was added NaOH (5.0 equivalents) and H_2O (0.11 M). The suspension was stirred at 40 °C for 25 min then concentrated *in vacuo*. The residue was dissolved in DMSO then filtered and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 55 to 75% of Mobile Phase B over 10.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide to give the desired target.

[s]: Additional Amide Coupling in last step: A reaction mixture of amine (1.0 equivalent), acid (1.1 equivalent), chloro-*N*,*N*,*N*',*N*'-tetramethylformamidinium hexafluorophosphate (1.5 equivalents) and 1-methylimidazole (3.5 equivalents) in ACN (0.08 M) were stirred at room temperature for ~24 h then diluted with H_2O (1 mL). The suspension was extracted with DCM (3 x 2 mL). The combined organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. The residue was suspended in DMSO then filtered and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 60 to 80% of Mobile Phase B over 10.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide to give the desired target.

[t]: Additional Borylation step: A reaction mixture of bromo-substituted heterocycle (1.0 equivalents), bis(pinacolato)diborane (1.6 equivalents), Pd(dppf)Cl_2 (0.1 equivalent) and potassium acetate (3.0 equivalents) in dioxane (0.16 M) was degassed with nitrogen gas for 10 min then stirred at 80 °C for 17 h. The suspension was concentrated in vacuo then purified by column chromatography (silica gel, 0-100% EtOAc: heptane then 0-10% MeOH: EtOAc) to provide to give the desired target.

[u]: Additional Palladium coupling: To a reaction mixture of Na_2CO_3 (3.00 equivalent), borylate-substituted heterocycle (1.00 equivalents) and $Pd(dppf)Cl_2$ (0.10 equivalents) in dioxane (0.07 M) and H_2O (0.5 M) was added bromo-substituted heterocycle (1.15 equivalents). The suspension was degassed with nitrogen gas for a few minutes then stirred at 80 °C for ~24 h and filtered over celite. The filtrate was concentrated *in vacuo* and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 35 to 55% of Mobile Phase B over 10.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide to give the desired target.

[v]: Additional Palladium coupling: To a reaction mixture of Na_2CO_3 (3.00 equivalent), borylate-substituted heterocycle (1.00 equivalents) and $Pd(dppf)Cl_2$ (0.10 equivalents) in dioxane (0.07 M) and H_2O (0.5 M) was added bromo-substituted heterocycle (1.15 equivalents). The suspension was degassed with nitrogen gas for a few minutes then stirred at 80 °C for ~24 h and filtered over celite. The filtrate was concentrated *in vacuo* and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 35 to 55% of Mobile Phase B over 10.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide to give the desired target.

[w]: SNAr altered: To a reaction mixture of amine (1.0 equivalent) and fluoro and borylate-substituted heterocycle (2.0 equivalents) in ACN (0.1 M) and DMSO (1.0 M) was added TEA (10.0 equivalents). The reaction was stirred at 80 °C for 48 h then the crude mixture was used directly in the next step.

[x]: Additional Palladium coupling: A reaction mixture of K_2CO_3 (5.00 equivalent), boronic acid-substituted heterocycle (1.50 equivalents), $Pd(dppf)Cl_2$ (0.10 equivalent) and APhos Pd G3 (0.10 equivalents) was degassed with nitrogen gas then suspended in dioxane (0.04 M) and H_2O (0.15 M). The reaction mixture was stirred at 70 °C for 1 h and 30 min then concentrated *in vacuo*. The residue was dissolved in DMSO, filtered and purified by reverse phase HPLC (Sunfire C_{18} 100 mm x 19 mm x 5 µm column, Mobile Phase A: H_2O/ Mobile Phase B: ACN (0.05% TFA), 60 to 95% of Mobile Phase B over 10.0 min, 95% of Mobile Phase B hold 1.0 min, flow rate: 25 mL/min) to provide to give the desired target.

[y]: Additional Palladium coupling: A reaction mixture of K_2CO_3 (4.00 equivalent), boronic acid-substituted heterocycle (1.00 equivalents), *N*-XantPhos Pd G3 (0.10 equivalent) and bromo-substituted heterocycle (1.50 equivalents) was degassed with nitrogen gas then suspended in dioxane (0.04 M) and H_2O (0.15 M). The reaction mixture was stirred at room temperature for 72 h then stirred to 50 °C for 2 h. To the suspension was added an additional portion of *N*-XantPhos Pd G3 (0.10 equivalent) then stirred to 50 °C for 2 h. The reaction mixture was stirred at 90 °C for 1 h then concentrated *in vacuo* to provide to give the desired target.

Chiral Purification Data:

Example 50^: The chiral purity was determined using SFC analytical method on Chiralpak AD-3, 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; isocratic 40% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **50** ((SFC-MS) *m/z* $(M+H)^+$ = 519.37 at retention time: 2.047 min, 100% ee).

Example 51^: A crude mixture was separated into its component isomers using SFC purification [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate: 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OJ-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; gradient: 5-40% of Mobile Phase B in 1.5 min and hold 40% for 1.0 min then 5% of Mobile Phase B for 0.5 min; flow rate: 3.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **51** ((SFC-MS) *m/z* $(M+H)^+$ = 519.46 at retention time: 1.735 min, 100% ee).

Example 53 and 54^: A mixture of Example **53** and Example **54** were separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% isopropyl alcohol with 0.1% of NH_4OH; flow rate: 80 mL/ min; gradient time: 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropanol with 0.05% of DEA; isocratic: 40% of Mobile Phase B; flow rate: 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **54**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 519.30 at retention time: 2.019 min, 100% ee) and Example **53**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 519.28 at retention time: 3.607 min, 100% ee).

Example 58 and 78^: Example **77** was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% MeOH (0.1% NH_4OH); flow rate: 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH with 0.2% of NH_3; isocratic: 40% of Mobile Phase B; flow rate: 3.5 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **58**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 533.41 at retention time: 0.778 min, 100% ee) and Example **78**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 533.41 at retention time: 1.392 min, 100% ee).

Example 63^: A mixture was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH with 0.1% of NH_4OH; flow rate: 60 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.05% of DEA; isocratic: 40% of Mobile Phase B; flow rate:

4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **63:** peak 1 (retention time: 0.710 min, 100% ee) and peak 2 (retention time: 1.175 min, 100% ee).

Example 82 and 83^: A crude material was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% isopropyl alcohol (0.1% NH_4OH); flow rate= 80 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol with 0.05% of DEA; isocratic: 40% of Mobile Phase B; flow rate: 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **82**: peak 1 (retention time: 1.233 min, 100% ee) and Example **83**: peak 2 (retention time: 1.622 min, 97% ee).

Example 87 and 237^: Example **62** was separated into its component isomers using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% isopropyl alcohol (0.1% NH_4OH); flow rate= 150 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3, 50 mm x 4.6 mm x 3 µm; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% NH_3; isocratic gradient: 40% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **237**: peak 1 ((SFC-MS) retention time: 2.293 min, 100% ee) and Example **87**: peak 2 ((SFC-MS) retention time: 3.434 min, 100% ee)

Example 111^: A crude material was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3, 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol with 0.05% DEA; isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **111**: peak 1 ((SFC-MS) retention time: 4.224 min, 91% ee).

Example 112 and 128^: Example **95** was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% NH_3; isocratic gradient: 40% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **112**: peak 1 ((SFC-MS) m/z $(M+H)^+$ = 547.43 at retention time: 0.764 min, 100% ee) and Example **128**: peak 2 ((SFC-MS) m/z $(M+H)^+$ = 547.44 at retention time: 1.380 min, 100% ee).

Example 117 and 118^: Example **116** was separated into its component isomers using SFC [Column: Chiral Technologies OJ-H 250 mm x 21 mm x 5 µm; Mobile phase A: 85% CO_2; Mobile Phase B: 15% MeOH (0.2% NH_4OH); isocratic: 15% of Mobile Phase B; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies OJ-H 100 mm x 4.6 mm x 5 µm column;

Mobile phase A: 75% CO_2, Mobile phase B: 25% MeOH with 0.2% of NH_4OH; isocratic: 25% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time= 5 min to provide Example **117**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 547.3 at retention time: 2.61 min) and Example **118**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 547.3 at retention time: 2.98 min).

Example 119 and 557^: A crude material was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH with 0.1% of NH_4OH; flow rate= 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.05% of DEA; isocratic: 40% of Mobile Phase B; flow rate: 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **557**: peak 1 (retention time: 0.784 min, 100% ee) and Example **119**: peak 2 (retention time: 1.425 min, 100% ee).

Example 122^: A crude material was purified using SFC [Column: DAICEL CHIRALCEL OJ 250 mm x 30 mm x 10 µm; Mobile phase: 65% CO_2/ 35% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol (0.2% NH_3); isocratic gradient: 50% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **122**: peak 1 ((SFC-MS) m/z $(M+H)^+$ = 528.44 at retention time: 1.045 min, 100% ee).

Example 123 and 124^: A crude material was separated into its component isomers using SFC [Column: Chiral Technologies OJ-H 250 mm x 21 mm x 5 µm; Mobile phase A: 80% CO_2; Mobile Phase B: 20% MeOH with 0.2% of NH_4OH; isocratic: 20% of Mobile Phase B; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies OJ-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: 80% CO_2, Mobile phase B: 20% MeOH with 0.2% of NH_4OH; isocratic: 20% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time= 5 min to provide Example **123:** peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 581.3 at retention time: 2.37 min) and Example **124**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 581.3 at retention time: 4.00 min).

Example 127 and 552^: Example **532** was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2 with ACN/ 50% MeOH with 0.1% NH_4OH; flow rate= 150 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **127**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 548.51 at retention time: 1.085 min, 100% ee) and Example **552**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 548.51 at retention time: 1.489 min, 100% ee).

Example 131 and 336^: Example **130** was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH with 0.1% of NH_4OH; flow

rate= 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; isocratic: 40% of Mobile Phase B; flow rate: 3.5 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **131**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 533.44 at retention time: 0.973 min, 99% ee) and Example **336**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 533.45 at retention time: 1.841 min, 100% ee).

Example 190 and 191^: Example **90** was separated into its component isomers using SFC [Column: DAICEL CHIRALPAK IG 250 mm x 30 mm x 10 µm; Mobile phase: 80% MeOH/ 20% ACN; flow rate= 100 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak IG-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: MeOH (0.05% of DEA); Mobile phase B: ACN; isocratic gradient: 20% of Mobile Phase B; flow rate: 1.0 mL/min; column temperature: 35 °C to provide Example **190**: peak 1 ((SFC-MS) retention time: 3.431 min, 100% ee) and Example **191**: peak 2 ((SFC-MS) retention time: 4.646 min, 100% ee).

Example 203 and 204^: Example **59** was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min, gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.05% of DEA); gradient: 5- 40% of Mobile Phase B in 1.5 min and hold at 40% of Mobile Phase B for 1.0 min then 5% of Mobile phase B for 0.5 min; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **204**: peak 1 ((SFC-MS) m/z (M+H)+ = 528.17 at retention time: 2.106 min, 100% ee) and Example **203**: peak 2 ((SFC-MS) m/z (M+H)+ = 528.17 at retention time: 2.407 min, 99% ee).

Example 230 and 231^: A mixture was separated into its component isomers using SFC [Column: Lux Cellulose 1 250 mm x 21 mm x 5 µm; Mobile phase: 35% MeOH (0.2% NH_4OH)/ 65% ACN; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Lux Cellulose 1 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 50% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **230:** peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 545.2 at retention time: 2.92 min) and Example **231:** peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 545.3 at retention time: 3.87 min).

Example 232 and 233^: Example **205** was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min, gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.05% of DEA); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide

Example **233:** peak 1 ((SFC-MS) retention time: 0.883 min, 100% ee) and Example **232**: peak 2 ((SFC-MS) retention time: 1.583 min, 100% ee).

Example 234 and 235^: Example **85** was separated into its component isomers using SFC [Column: Chiral Technologies AD-H 250 mm x 30 mm x 5 µm; Mobile phase: 55% CO_2/ 45% 2-propanol (0.2% isopropylamine); flow rate= 80 mL/ min, backpressure= 120 bar, temperature= 40 °C]. The chiral purity was determined using SFC analytical method on Chiral Technologies AD-H 250 mm x 4.6 mm x 5 µm column; Mobile phase A: CO_2; Mobile phase B: 2-propanol (0.2% isopropylamine); gradient: 5-60% of Mobile Phase B over 8.0 min then 5% of Mobile Phase B over 0.50 min; flow rate: 3.0 mL/min; column temperature: 40 °C, backpressure: 120 bar to provide Example **234**: peak 1 ((SFC-MS) retention time: 7.391 min, 100% ee) and Example **235**: peak 2 ((SFC-MS) retention time: 7.794 min, 97% ee).

Example 250 and 251^: A mixture was separated into its component isomers using SFC [Column: Lux Cellulose 3 250 mm x 21 mm x 5 µm; Mobile phase: 20% MeOH (0.2% NH_4OH)/ 80% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Lux Cellulose 3 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 75% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **250**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 587.2 at retention time: 2.12 min) and Example **251**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 587.2 at retention time: 2.97 min).

Example 258 and 556^:A crude material was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.05% DEA); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **556**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 589.23 at retention time: 0.998 min, 100% ee) and Example **258**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 589.19 at retention time: 1.724 min, 100% ee).

Example 262 and 553^: A crude material was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min; gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.05% DEA); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **553**: peak 1 ((SFC-MS) retention time: 0.487 min, 100% ee) and Example **262**: peak 2 ((SFC-MS) retention time: 0.799 min, 100% ee).

Example 267 and 268^: Example **249** was separated into its component isomers using SFC [Column: Pirkle Covalent (R,R) Whelk-O1 250 mm x 21.1 mm x 5 µm; Mobile phase: 40% MeOH (0.2% NH_4OH)/ 60% ACN; flow rate= 75 mL/ min, gradient time= 40 min, backpressure=

120 bar]. The chiral purity was determined using SFC analytical method on Regis (R,R) Whelk-01 50 mm x 5 mm x 3 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 55% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 10 min to provide Example **267**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 561.2 at retention time: 3.23 min) and Example **268**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 561.2 at retention time: 2.72 min).

Example 269 and 270^: Example **260** was purified using SFC [Column: DAICEL CHIRALPAK IF 250 mm x 30 mm x 10 µm; Mobile phase: 30% heptane/ 70% (4:1, isopropyl alcohol: ACN) with 0.1% NH_4OH; flow rate= 80 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak IF 100 mm x 4.6 mm x 3 µm column; Mobile phase A: hexane (0.1% DEA); Mobile phase B: (2:1, isopropyl alcohol: ACN); isocratic gradient: 60% of Mobile Phase B; flow rate: 1.0 mL/min; column temperature: 35 °C to provide Example **269**: peak 1 ((SFC-MS) retention time: 3.315 min, 100% ee) and Example **270**: peak 2 ((SFC-MS) retention time: 6.412 min, 100% ee)

Example 271 and 272^: Example **265** was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **271**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 547.21 at retention time: 1.545 min, 100% ee) and Example **272**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 547.21 at retention time: 3.340 min, 100% ee).

Example 273^: A crude material was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% isopropyl alcohol (0.1% NH_4OH); flow rate= 150 mL/ min; gradient time= 4 min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **273**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 520.15 at retention time: 1.272 min, 100% ee).

Example 274 and 275^: Example **68** was purified using SFC [Column: CHIRALPAK IH 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 140 mL/ min, gradient time= 4 min]. The chiral purity was determined using SFC analytical method on Chiralpak AS-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); gradient: 5- 40% of Mobile Phase B in 2.0 min then hold for 40% of Mobile Phase B in 1.2 min then 5% of Mobile Phase B for 0.8 min; flow rate: 3.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **275**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 545.16 at retention time: 2.593 min, 99% ee) and Example **274**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 545.17 at retention time: 3.311 min, 100% ee).

Example 276 and 277^:Example **255** was separated into its component isomers using SFC [Column: Lux Cellulose 3 250 mm x 21 mm x 5 µm; Mobile phase: 15% MeOH (0.2% NH_4OH)/ 85% ACN; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Lux Cellulose 3 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 80% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **276**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 601.2 at retention time: 2.90 min) and Example **277**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 601.2 at retention time: 3.90 min).

Example 280 and 281^: A mixture was separated into its component isomers using SFC [Column: Lux Cellulose 1 250 mm x 21 mm x 5 µm; Mobile phase: 40% MeOH (0.2% NH_4OH)/ 60% ACN; flow rate= 75 mL/ min, gradient time= 40 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Lux Cellulose 1 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 40% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 10 min to provide Example **280**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 531.2 at retention time: 4.84 min) and Example **281**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 531.2 at retention time: 6.81 min).

Example 285 and 551^: A mixture was purified using SFC [Column: YMC-IB 250 mm x 30 mm x 10 µm; Mobile phase: 70% heptane/ 30% (4:1, isopropyl alcohol: ACN) with 0.1% NH_4OH; flow rate= 100 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak IB-N 100 mm x 4.6 mm x 3 µm column; Mobile phase A: hexane (0.1% DEA); Mobile phase B: (2:1, isopropyl alcohol: ACN); isocratic gradient: 40% of Mobile Phase B; flow rate: 1.0 mL/min; column temperature: 35 °C to provide Example **551**: peak 1 ((SFC-MS) retention time: 4.066 min, 100% ee) and Example **285**: peak 2 ((SFC-MS) retention time: 4.601 min, 99% ee).

Example 287^: A crude material was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min; gradient time= 45 min] to provide Example **287**. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; gradient: 5-40% of Mobile Phase B over 2.0 min and held at 40% of Mobile Phase B for 1.2 min then % of Mobile Phase B for 0.8 min; flow rate: 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **287**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 559.20 at retention time: 2.903 min, 100% ee).

Example 303 and 304^: Example **282** was separated into its component isomers using SFC [Column: Chiral Technologies OJ-H 250 mm x 21 mm x 5 µm; Mobile phase: 25% MeOH (0.2% NH_4OH)/ 75% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies OJ-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 70% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **303**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 587.2 at

retention time: 1.92 min) and Example **304**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 587.2 at retention time: 2.74 min).

Example 307 and 550^: A mixture was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% MeOH (0.1% NH_4OH); flow rate= 80 mL/ min, gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH (0.2% NH_3); gradient: 5- 40% of Mobile Phase B in 1.5 min and hold at 40% of Mobile Phase B for 1.0 min then 5% of Mobile phase B for 0.5 min; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **550**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 587.19 at retention time: 1.669 min, 100% ee) and Example **307**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 587.16 at retention time: 1.945 min, 100% ee).

Example 310 and 311^: Example **246** was separated into its component isomers using SFC [Column: Chiral Technologies IB 250 mm x 21 mm x 5 µm; Mobile phase: 40% MeOH (0.2% NH_4OH)/ 60% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies IB 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 50% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **310**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 561.3 at retention time: 2.14 min) and Example **311**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 561.3 at retention time: 3.12 min).

Example 312 and 313^: Example **115** was separated into its component isomers using SFC [Column: Chiral Technologies IB 250 mm x 21 mm x 5 µm; Mobile phase: 40% MeOH (0.2% NH_4OH)/ 60% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies IB 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 50% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **312**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 547.3 at retention time: 2.40 min) and Example **313**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 547.3 at retention time: 3.61 min).

Example 316 and 317^: Example **314** was separated into its component isomers using SFC [Column: Lux Cellulose 1 250 mm x 21 mm x 5 µm; Mobile phase: 35% MeOH (0.2% NH_4OH)/ 65% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Lux Cellulose 1 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 60% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **316**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 547.2 at retention time: 2.40 min) and Example **317**: peak 3 ((SFC-MS) *m/z* $(M+H)^+$ = 547.2 at retention time: 2.94 min).

Example 318 and 319^:A crude material was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% isopropyl alcohol (0.1% NH_4OH); flow rate= 150 mL/ min]. The chiral purity was determined using SFC analytical

method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **318**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 561.20 at retention time: 1.188 min, 100% ee) and Example **319**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 561.22 at retention time: 1.900 min, 99% ee).

Example 335 and 549^: A crude material was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% EtOH (0.1% NH_4OH); flow rate= 150 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **549:** peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 528.18 at retention time: 0.811 min, 99% ee) and Example **335**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 528.25 at retention time: 1.497 min, 100% ee).

Example 347 and 348^: Example **358** was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% isopropyl alcohol (0.1% NH_4OH); flow rate= 150 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **347**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 558.17 at retention time: 1.067 min, 100% ee) and Example **348**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 558.21 at retention time: 1.503 min, 98% ee).

Example 352 and 353^: The crude mixture was separated into its component isomers using SFC [Column: Chiral Technologies IH 250 mm x 21 mm x 5 µm; Mobile phase: 35% MeOH (0.2% NH_4OH)/ 65% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies IH 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 60% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **352**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 547.2 at retention time: 1.97 min) and Example **353**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 547.3 at retention time: 3.05 min).

Example 354 and 355^: Example **315** was separated into its component isomers using SFC [Column: Chiral Technologies OD-H 250 mm x 21 mm x 5 µm; Mobile phase: 25% MeOH (0.2% NH_4OH)/ 75% ACN; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies OD-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 60% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **354**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 561.4 at

retention time: 2.67 min) and Example **355**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 561.3 at retention time: 3.19 min).

Example 356 and 357^: The crude mixture was separated into its component isomers using SFC [Column: Chiral Technologies OJ-H 250 mm x 21 mm x 5 µm; Mobile phase: 20% MeOH (0.2% NH_4OH)/ 80% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies OJ-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 75% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **356**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 572.2 at retention time: 1.78 min) and Example **357**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 572.2 at retention time: 3.51 min).

Example 359 and 360^: Example **351** was purified using SFC [Column: DAICEL CHIRALPAK IF 250 mm x 30 mm x 10 µm; Mobile phase: 50% heptane/ 50% (4:1, isopropyl alcohol: ACN); flow rate= 100 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak IF 100 mm x 4.6 mm x 3 µm column; Mobile phase A: hexane (0.1% DEA); Mobile phase B: (2:1, isopropyl alcohol: ACN); isocratic gradient: 60% of Mobile Phase B; flow rate: 1.0 mL/min; column temperature: 35 °C to provide Example **359**: peak 1 ((SFC-MS) retention time: 3.568 min, 100% ee) and Example **360**: peak 2 ((SFC-MS) retention time: 4.561 min, 98% ee).

Example 361 and 362^: Example **322** was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; isocratic: 40% of Mobile Phase B; flow rate: 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **361**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 532.18 at retention time: 0.818 min, 100% ee) and Example **362**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 532.21 at retention time: 1.180 min, 99% ee).

Example 391 and 392^: The crude mixture was separated into its component isomers using SFC [Column: Chiral Technologies OJ-H 250 mm x 21 mm x 5 µm; Mobile phase: 30% MeOH (0.2% NH_4OH)/ 70% ACN; flow rate= 75 mL/ min, gradient time= 10 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies OJ-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 65% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide Example **391**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 573.2 at retention time: 1.93 min) and Example **392**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 573.2 at retention time: 3.20 min).

Example 393 and 394^: Example **339** was purified using SFC [Column: DAICEL CHIRALCEL OJ 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralcel OJ-3

50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 3.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **393**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 546.64 at retention time: 0.895 min, 100% ee) and Example **394**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 546.63 at retention time: 1.939 min, 99% ee).

Example 428 and 429^: Example **399** was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min, gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **428**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 532.22 at retention time: 0.636 min, 100% ee) and Example **429**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 532.21 at retention time: 1.130 min, 100% ee).

Example 444 and 445^: Example **55** was purified using SFC [Column: ChiralPak IH 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% EtOH (0.1% NH_4OH); flow rate= 150 mL/ min, gradient time= 4 min]. The chiral purity was determined using SFC analytical method on Chiralpak AS-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 3.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **444**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 519.62 at retention time: 1.191 min, 100% ee) and Example **445**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 519.62 at retention time: 1.728 min, 99% ee).

Example 446 and 447^: The crude mixture was separated into its component isomers using SFC [Column: Chiral Technologies IA 250 mm x 21 mm x 5 µm; Mobile phase: 40% MeOH (0.2% NH_4OH)/ 60% ACN; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies IA 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 45% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 10 min to provide Example **446**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 548.3 at retention time: 2.33 min) and Example **447**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 548.3 at retention time: 6.75 min).

Example 448 and 449^: The crude mixture was separated into its component isomers using SFC [Column: Chiral Technologies IA 250 mm x 21 mm x 5 µm; Mobile phase: 35% MeOH (0.2% NH_4OH)/ 65% ACN; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies IA 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 45% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 10 min to provide Example **448**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 562.3 at

retention time: 1.96 min) and Example **449**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 562.3 at retention time: 4.38 min).

Example 461 and 462^: Example **459** was separated into its component isomers using chiral HPLC purification [Column: C_{18} 150 mm x 40 mm; Mobile phase: H_2O (NH_4OH-NH_4HCO_3)/ACN; gradient= 13-53% of Mobile Phase B; flow rate= 60 mL/ min, gradient time= 9 min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **461**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 602.71 at retention time: 0.837 min, 100% ee) and Example **462**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 602.70 at retention time: 1.799 min, 100% ee).

Example 464 and 465^: Example **460** was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% EtOH (0.1% NH_4OH); flow rate= 150 mL/ min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: isopropyl alcohol (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **464**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 588.69 at retention time: 0.715 min, 100% ee) and Example **465**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 588.67 at retention time: 2.128 min, 98% ee).

Example 467 and 468^: Example **463** was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% MeOH (0.1% NH_4OH); flow rate= 80 mL/ min, gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **467**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 558.47 at retention time: 0.408 min, 100% ee) and Example **468**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 558.48 at retention time: 0.707 min, 99% ee).

Example 474 and 475^: Example **472** was purified using SFC [Column: DAICEL CHIRALPAK AD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% MeOH (0.1% NH_4OH); flow rate= 80 mL/ min, gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralpak AD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **474**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 549.68 at retention time: 0.836 min, 100% ee) and Example **475**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 549.68 at retention time: 2.047 min, 100% ee).

Example 493 and 494^: The crude mixture was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% MeOH (0.1% NH_4OH); flow rate= 70 mL/ min, gradient time= 45 min, column temperature= 40 °C,

backpressure= 100 bar]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 3.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **493**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 583.71 at retention time: 0.784 min, 100% ee) and Example **494**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 583.69 at retention time: 1.855 min, 100% ee).

Example 506 and 507^: The crude mixture was purified using SFC [Column: DAICEL CHIRALPAK AS 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% (4:1, EtOH: ACN) (0.1% NH_4OH); flow rate= 150 mL/ min, gradient time= 40 min]. The chiral purity was determined using SFC analytical method on Chiralpak AS-3 100 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 2.8 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **506**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 547.25 at retention time: 1.151 min, 100% ee) and Example **507**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 547.22 at retention time: 2.043 min, 100% ee).

Example 508 and 509^: The crude mixture was purified using SFC [Column: DAICEL CHIRALPAK AS 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% (4:1, EtOH: ACN) (0.1% NH_4OH); flow rate= 150 mL/ min, gradient time= 60 min]. The chiral purity was determined using SFC analytical method on Chiralpak AS-3 100 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 2.8 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **508**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 548.26 at retention time: 1.285 min, 100% ee) and Example **509**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 548.31 at retention time: 3.523 min, 100% ee).

Example 510 and 511^: The crude mixture was purified using SFC [Column: DAICEL CHIRALPAK AS 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% (1:1, EtOH: ACN) (0.1% NH_4OH); flow rate= 140 mL/ min, column temperature= 40 °C, backpressure= 100 bar]. The chiral purity was determined using SFC analytical method on Chiralpak AS-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 50% of Mobile Phase B; flow rate: 2.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **510**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 534.55 at retention time: 0.702 min, 100% ee) and Example **511**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 534.58 at retention time: 1.561 min, 100% ee).

Example 514 and 515^: The crude mixture was purified using SFC [Column: DAICEL CHIRALPAK AS 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 140 mL/ min, column temperature= 40 °C, backpressure= 100 bar]. The chiral purity was determined using SFC analytical method on Chiralpak AS-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40%

of Mobile Phase B; flow rate: 3.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **514**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 533.56 at retention time: 0.979 min, 100% ee) and Example **515**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 533.56 at retention time: 1.597 min, 99% ee).

Example 527 and 528^: A crude material was purified using SFC [Column: DAICEL CHIRALPAK AS 250 mm x 30 mm x 10 µm; Mobile phase: 45% CO_2/ 55% EtOH (0.1% NH_4OH); flow rate= 140 mL/ min, backpressure= 100 bar, column temperature= 40 °C]. The chiral purity was determined using SFC analytical method on Chiralpak AS-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 50% of Mobile Phase B; flow rate: 2.5 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **527:** peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 561.59 at retention time: 0.509 min, 100% ee) and Example **528**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 561.59 at retention time: 1.377 min, 100% ee).

Example 529^: Example **524** was separated into its component isomers using SFC [Column: Phenomenex Lux Cellulose 1 250 mm x 21 mm x 5 µm; Mobile phase: 30% MeOH/ 70% ACN; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar, column temperature= 50 °C]. The chiral purity was determined using SFC analytical method on Lux Cellulose 1 100 mm x 4.6 mm x 5 µm column; Mobile phase A: MeOH; Mobile phase B: ACN; isocratic gradient: 60% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 5 min to provide peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 561.2 at retention time: 3.28 min) and Example **529**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 561.2 at retention time: 3.40 min).

Example 538 and 539^: Example **537** was purified using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); flow rate= 80 mL/ min, gradient time= 45 min]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH (0.2% NH_3); isocratic gradient: 40% of Mobile Phase B; flow rate: 4.0 mL/min; column temperature: 35 °C, backpressure: 1500 psi to provide Example **539**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 546.24 at retention time: 0.607 min, 100% ee) and Example **538**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 546.22 at retention time: 1.034 min, 100% ee).

Example 547 and 548^: Example **546** was separated into its component isomers using SFC [Column: Chiral Technologies OD-H 250 mm x 21 mm x 5 µm; Mobile phase: 40% CO_2/ 60% MeOH (0.2% NH_4OH); flow rate= 75 mL/ min, backpressure= 120 bar, gradient time= 10 min]. The chiral purity was determined using SFC analytical method on Chiral Technologies OD-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: CO_2; Mobile phase B: MeOH (0.2% NH_4OH); isocratic gradient: 50% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar to provide Example **548**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 601.3 at retention time: 1.99 min).and Example **547**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 601.3 at retention time: 3.94 min).

Example 667 and 668^: A mixture was separated into its component isomers using SFC [Column: Chiral Technologies AD-H 250 mm x 30 mm x 5 µm; Mobile phase: 60% CO_2/ 40% 2-propanol (0.2% isopropylamine); flow rate= 100 mL/ min, backpressure= 100 bar, temperature= 40 °C]. The chiral purity was determined using SFC analytical method on Chiral Technologies AD-H 250 mm x 4.6 mm x 5 µm column; Mobile phase A: CO_2; Mobile phase B: 2-propanol (0.2% isopropylamine); gradient: 5-100% of Mobile Phase B over 7.50 min then 5% of Mobile Phase B over 0.50 min; flow rate: 3.0 mL/min; column temperature: 40 °C, backpressure: 100 bar to provide Example **668**: peak 1 ((SFC-MS) retention time: 6.547 min, 99% ee) and Example **667**: peak 2 ((SFC-MS) retention time: 6.951 min, 96% ee).

Example 670 and 671^: A mixture was separated into its component isomers using SFC [Column: Chiral Technologies AS-H 250 mm x 21 mm x 5 µm; Mobile phase A: 25% CO_2; Mobile Phase B: 75% MeOH (0.2% NH_4OH); isocratic: 75% of Mobile Phase B; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies AS-H 100 mm x 4.6 mm x 5 µm column; Mobile phase A: 25% CO_2, Mobile phase B: 75% MeOH with 0.2% of NH_4OH; isocratic: 75% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time= 20 min to provide Example **671**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 645.4 at retention time: 8.71 min) and Example **670**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 645.3 at retention time: 13.48 min).

Example 672 and 673^: Example **710** was separated into its component isomers using SFC [Column: Chiral Technologies IB 250 mm x 21 mm x 5 µm; Mobile phase A: 35% CO_2; Mobile Phase B: 65% MeOH (0.2% NH_4OH); isocratic: 65% of Mobile Phase B; flow rate= 75 mL/ min, gradient time= 20 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Chiral Technologies IB 100 mm x 4.6 mm x 5 µm column; Mobile phase A: 40% CO_2, Mobile phase B: 60% MeOH with 0.2% of NH_4OH; isocratic: 60% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time= 10 min to provide Example **673**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 631.3 at retention time: 5.53 min) and Example **672**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 631.3 at retention time: 6.86 min).

Example 692 and 693^: Example **701** was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% EtOH (0.1% NH_4OH); isocratic: 50% of Mobile Phase B; flow rate: 80 mL/ min; backpressure= 100 bar, column temperature= 40 °C]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; gradient: 5-40% of Mobile Phase B in 2.0 min and hold 40% for 1.2 min then 5% of Mobile Phase B for 0.8 min; flow rate: 4.0 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **693**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 656.34 at retention time: 2.201 min, 100% ee) and Example **692**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 656.35 at retention time: 2.705 min, 100% ee).

Example 694 and 695^: Example **696** was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 40% CO_2/ 60% EtOH (0.1% NH_4OH); isocratic: 60% of Mobile Phase B; flow rate: 80 mL/ min; backpressure= 100 bar, column temperature= 40 °C]. The chiral purity was determined using SFC analytical method on Chiralcel OD-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; isocratic: 40% of Mobile Phase B; flow rate: 3.5 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **695**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 642.35 at retention time: 0.836 min, 100% ee) and Example **694**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 642.32 at retention time: 1.519 min, 100% ee).

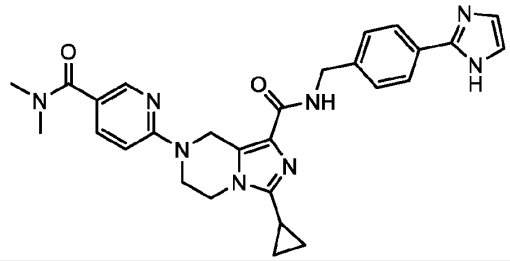
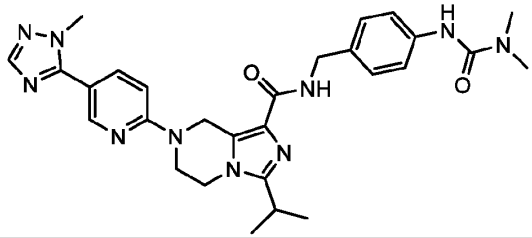
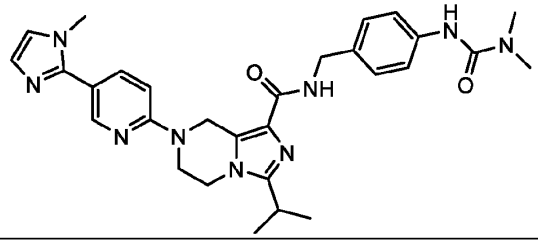
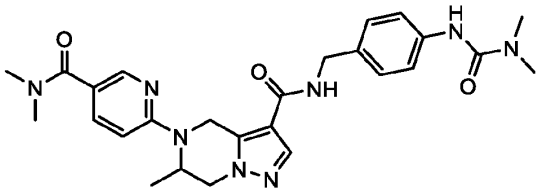
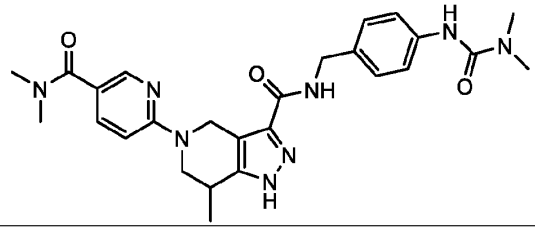
Example 702 and 705^: Example **703** was separated into its component isomers using SFC [Column: DAICEL CHIRALCEL OD 250 mm x 30 mm x 10 µm; Mobile phase: 50% CO_2/ 50% EtOH (0.1% NH_4OH); isocratic: 50% of Mobile Phase B; gradient time= 30 min; flow rate: 80 mL/ min]. The chiral purity was determined using SFC analytical method on IM-3 50 mm x 4.6 mm x 3 µm column; Mobile phase A: CO_2; Mobile phase B: EtOH with 0.2% of NH_3; isocratic: 50% of Mobile Phase B; flow rate: 3.5 mL/min; backpressure: 1500 psi; column temperature: 35 °C to provide Example **702**: peak 1 ((SFC-MS) *m/z* $(M+H)^+$ = 655.78 at retention time: 1.217 min, 100% ee) and Example **705**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 655.78 at retention time: 2.492 min, 100% ee).

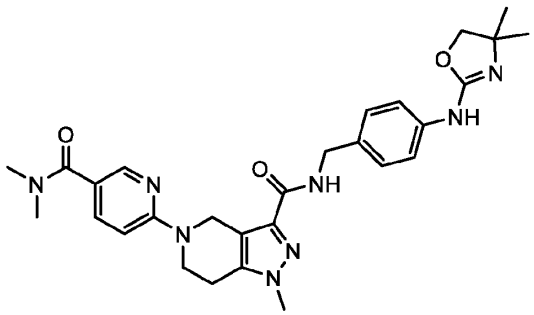
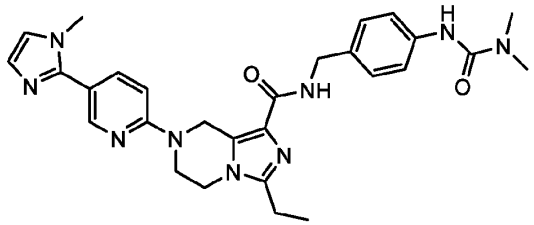
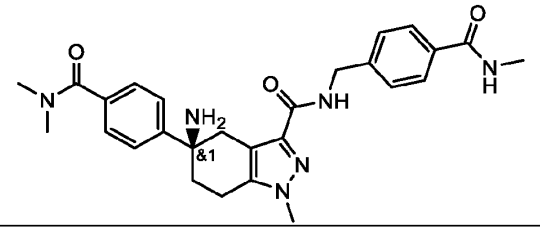
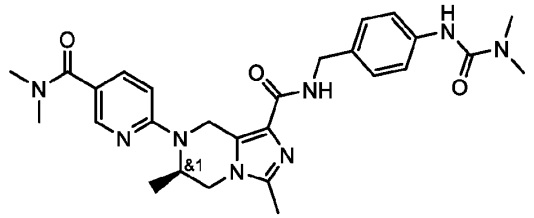
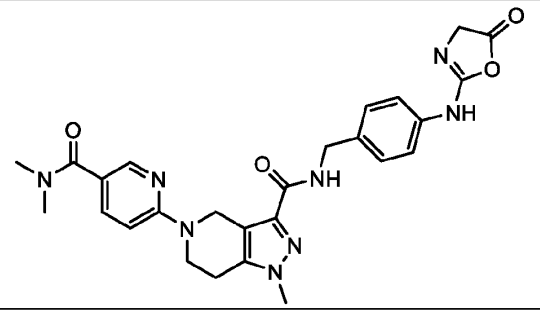
Example 713 and 714^: A mixture was separated into its component isomers using SFC [Column: Pirkle Covalent (R,R) Whelk-O1 250 mm x 21.1 mm x 5 µm; Mobile phase: 40% MeOH (0.2% NH_4OH)/ 60% ACN; flow rate= 75 mL/ min, gradient time= 70 min, backpressure= 120 bar]. The chiral purity was determined using SFC analytical method on Regis (R,R) Whelk-01 50 mm x 5 mm x 3 µm column; Mobile phase A: MeOH (0.2% NH_4OH); Mobile phase B: ACN; isocratic gradient: 60% of Mobile Phase B; flow rate: 5.0 mL/min; backpressure: 120 bar, gradient time: 30 min to provide Example **714**: peak 1 ((SFC-MS) *m/z* $(M/2+H)^+$ = 308.2 at retention time: 16.09 min) and Example **713**: peak 2 ((SFC-MS) *m/z* $(M+H)^+$ = 615.4 at retention time: 16.43 min).

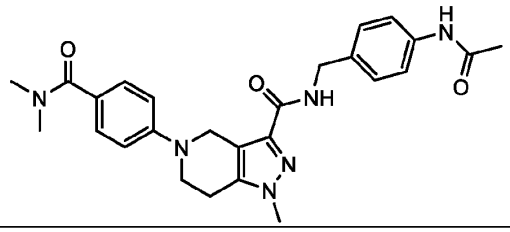
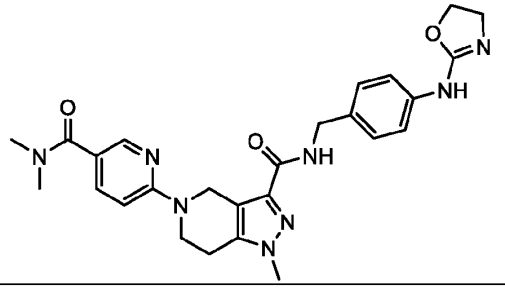
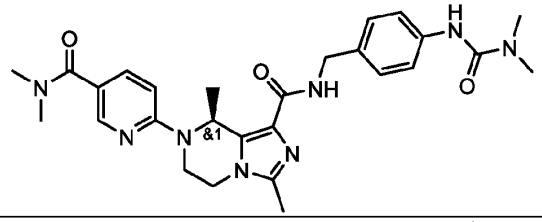
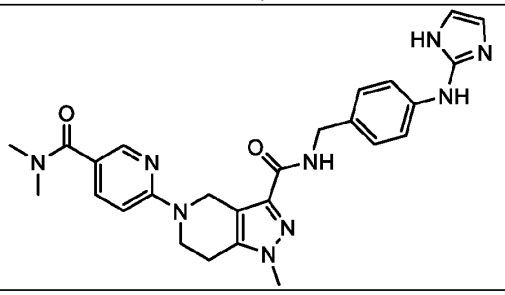
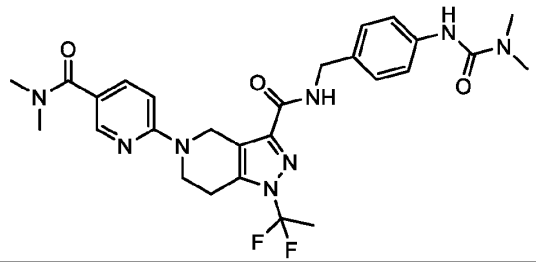
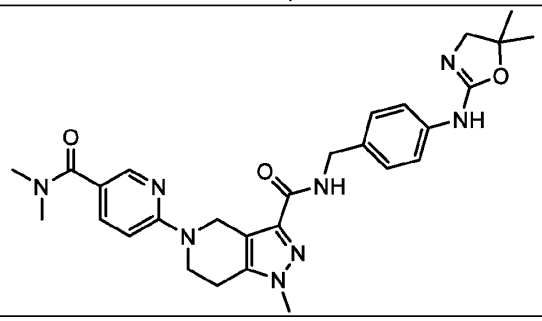
Examples V1-V142

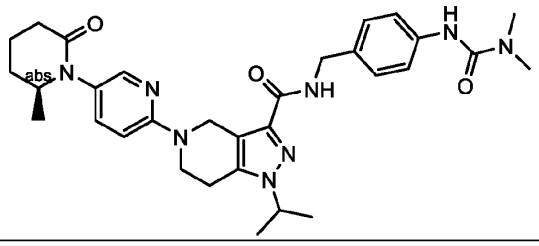
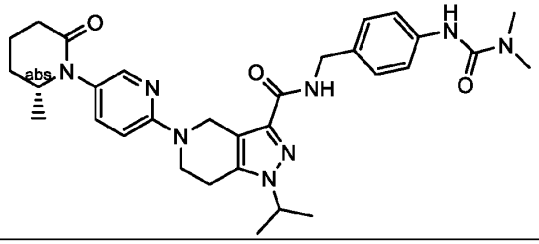
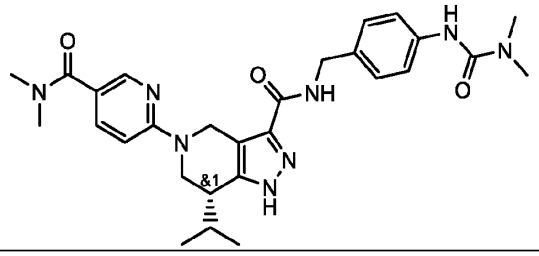
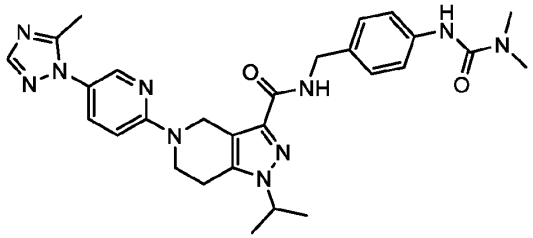
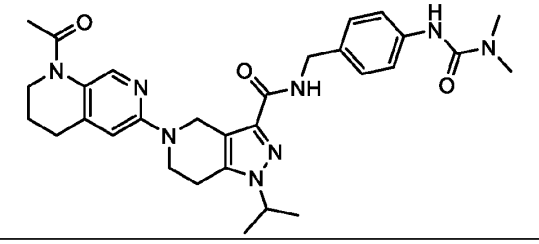
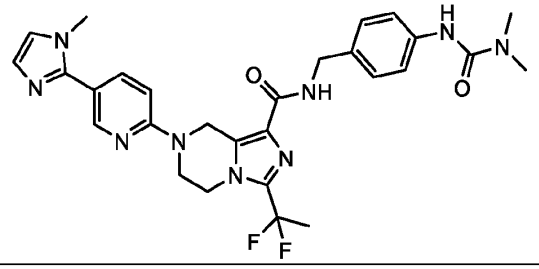
The compounds in Table 2 can be prepared using similar chemistry from Examples 1-758 that are commercially available or that can be synthesized by literature methods to form the resultant compounds of the disclosure.

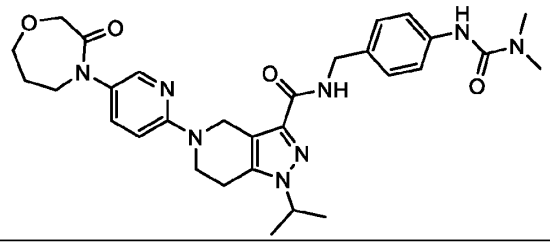
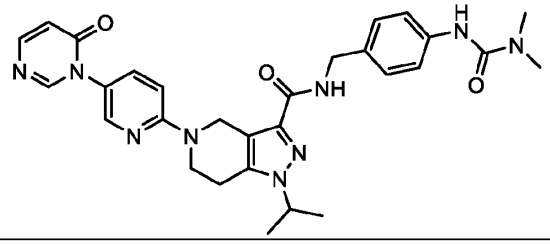
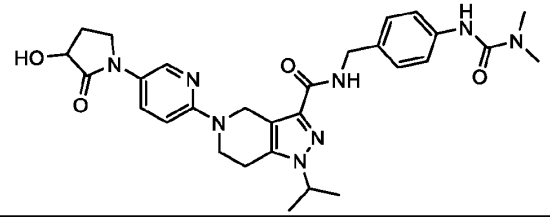
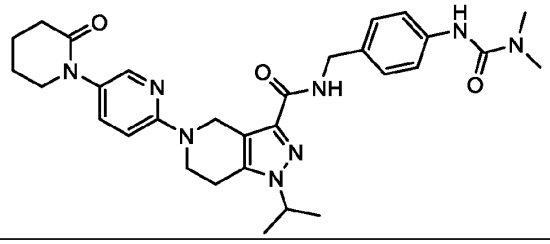
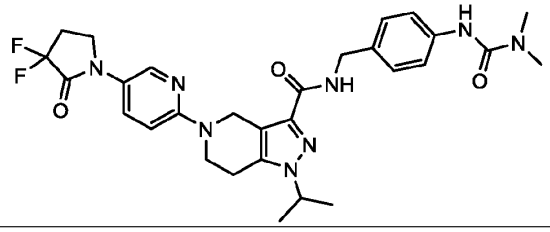
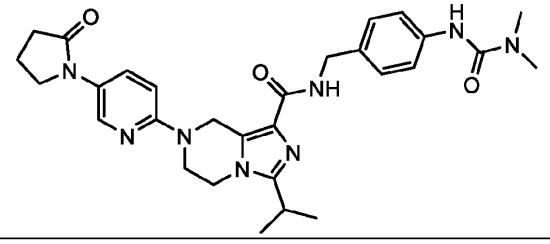
Table 2

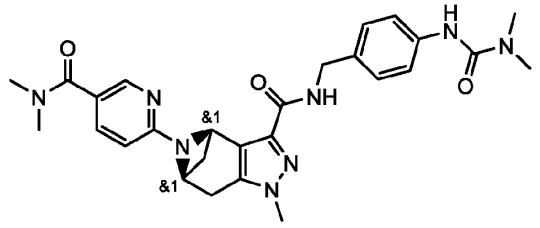
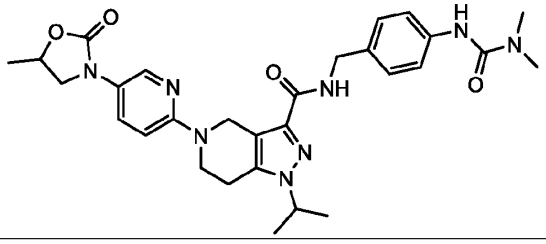
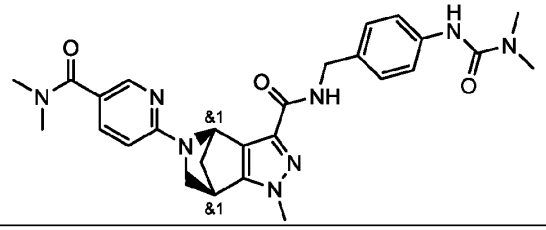
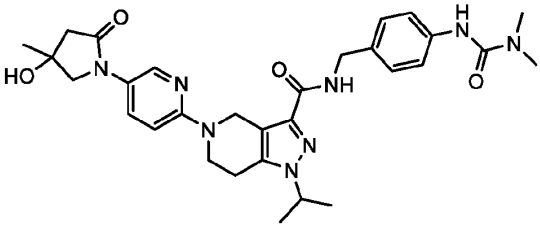
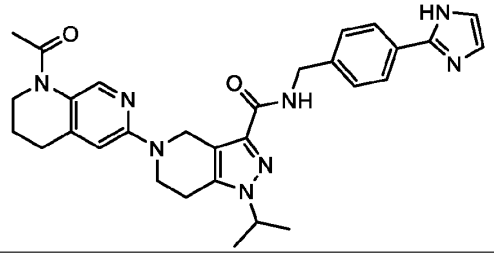
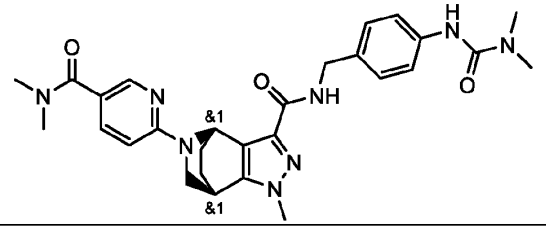
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V2		*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-7-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
V3		*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
V4		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-3-carboxamide
V5		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

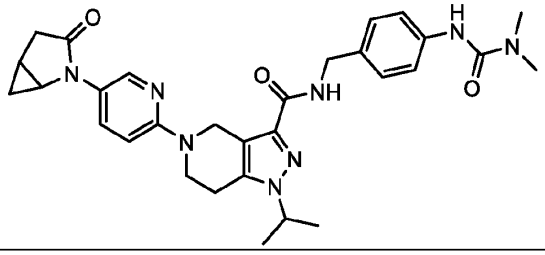
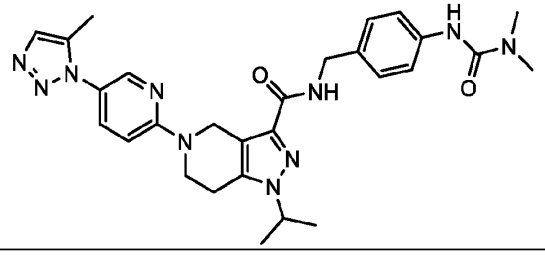
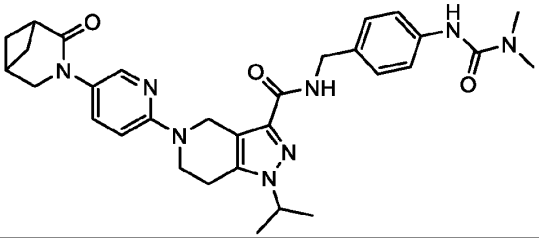
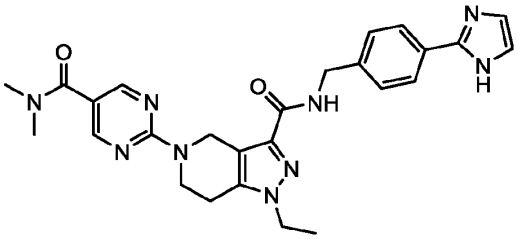
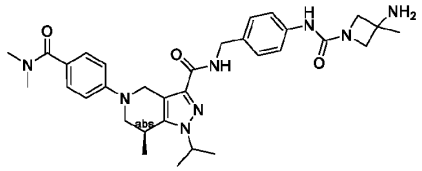
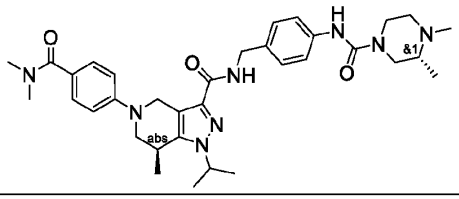
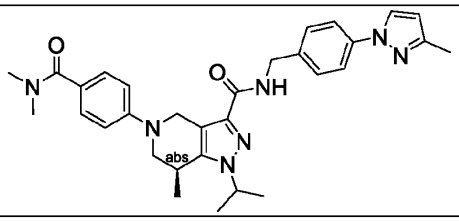
V6		*N*-(4-((4,4-dimethyl-4,5-dihydrooxazol-2-yl)amino)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V7		*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
V8		*rac*-(*R*)-5-amino-5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxamide
V9		*rac*-(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,6-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
V10		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-methyl-*N*-(4-((5-oxo-4,5-dihydrooxazol-2-yl)amino)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

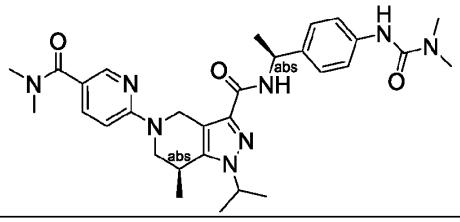
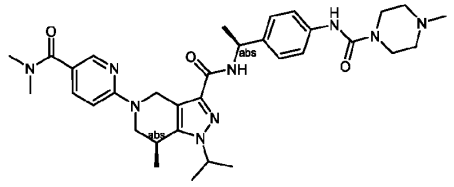
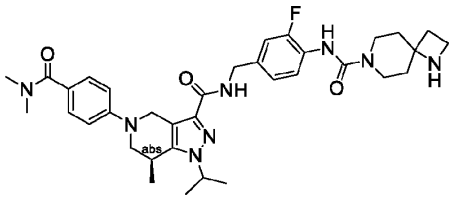
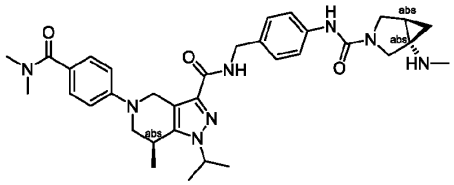
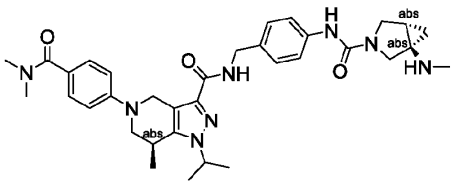
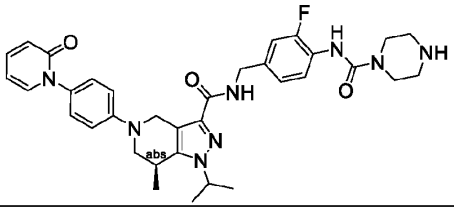
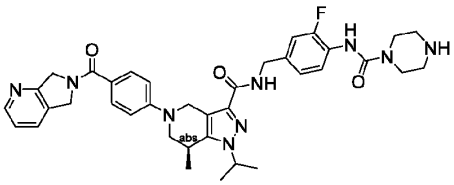
V11		*N*-(4-acetamidobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V12		*N*-(4-((4,5-dihydrooxazol-2-yl)amino)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V13		*rac*-(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,8-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
V14		*N*-(4-((1*H*-imidazol-2-yl)amino)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V15		1-(1,1-difluoroethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V16		*N*-(4-((5,5-dimethyl-4,5-dihydrooxazol-2-yl)amino)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

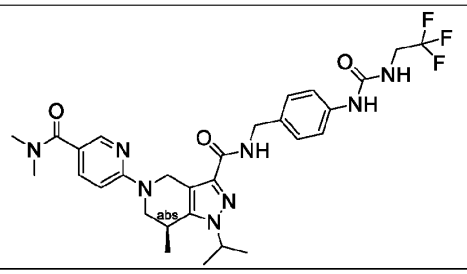
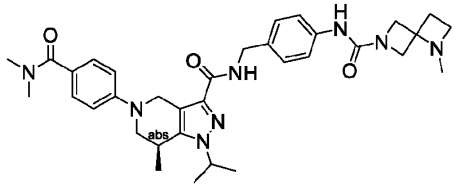
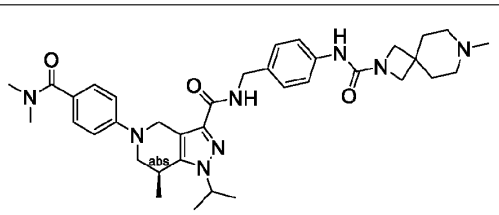
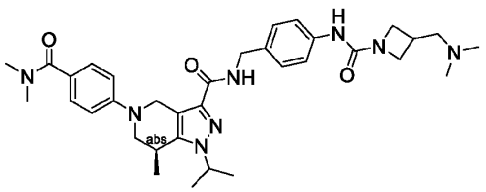
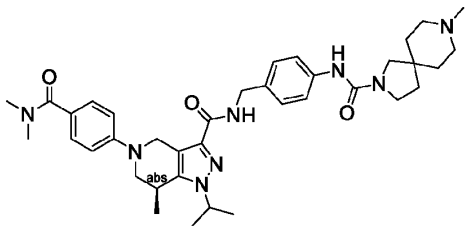
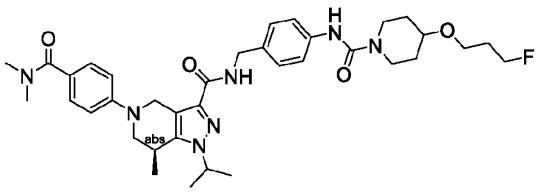
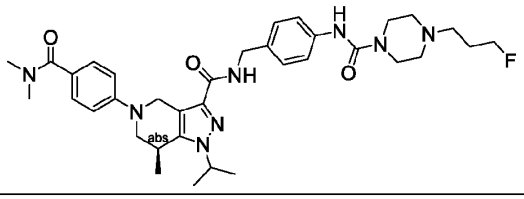
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V18		(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-6-oxopiperidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V19		*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V20		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-methyl-1*H*-1,2,4-triazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V21		5-(1-acetyl-1,2,3,4-tetrahydro-1,7-naphthyridin-6-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V22		3-(1,1-difluoroethyl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide

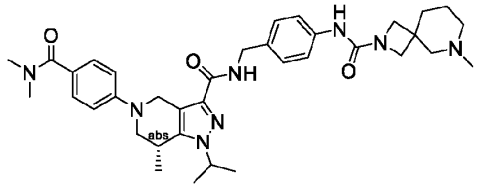
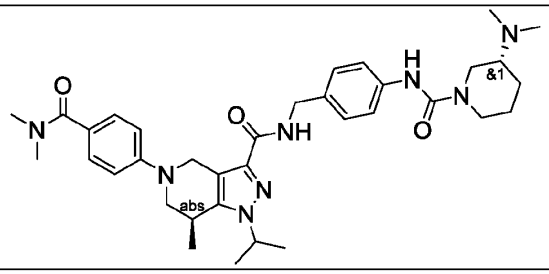
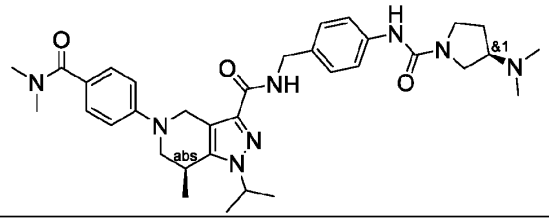
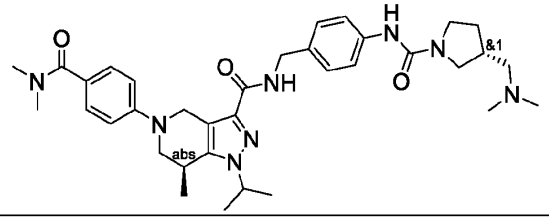
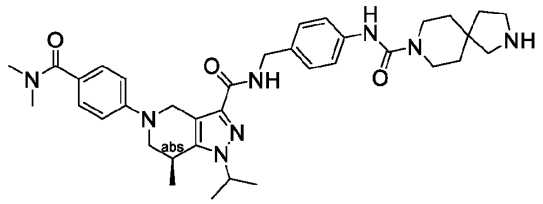
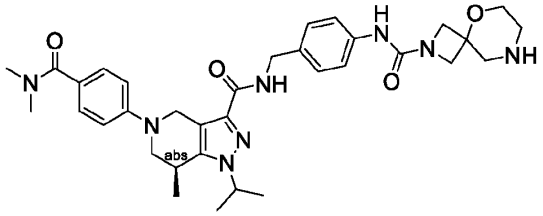
V23		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxo-1,4-oxazepan-4-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V24		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxopyrimidin-1(6*H*)-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V25		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxy-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V26		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopiperidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V27		5-(5-(3,3-difluoro-2-oxopyrrolidin-1-yl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V28		*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-7-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide

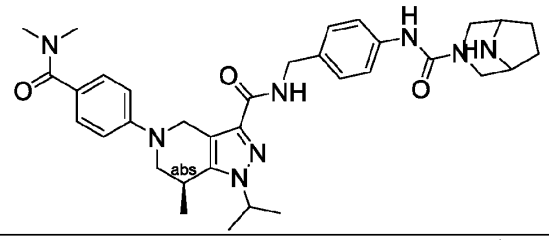
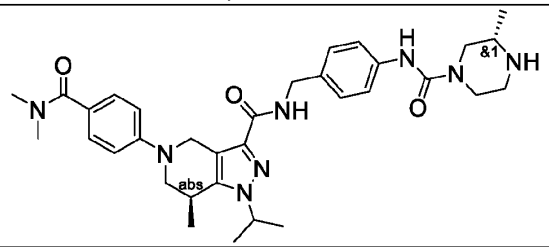
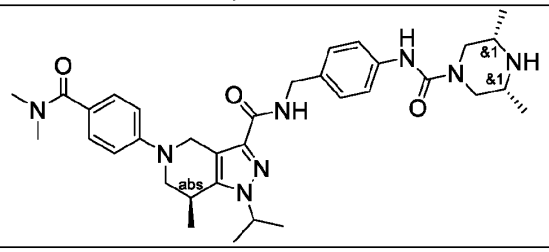
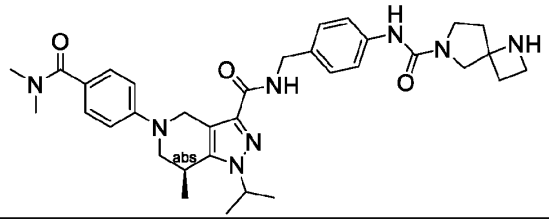
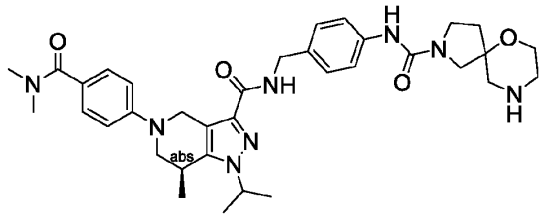
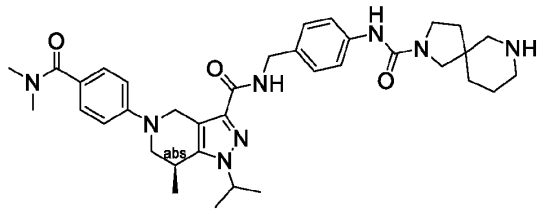
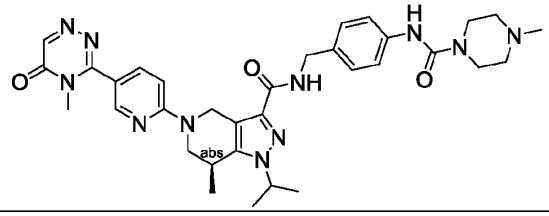
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V30		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-methyl-2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V31		*rac*-(4*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-4,7-methanopyrazolo[4,3-*c*]pyridine-3-carboxamide
V32		*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-hydroxy-4-methyl-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V33		*N*-(4-(1H-imidazol-2-yl)benzyl)-5-(1-acetyl-1,2,3,4-tetrahydro-1,7-naphthyridin-6-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V34		*rac*-(4*R*,7*R*)-9-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-4,7-(epiminomethano)indazole-3-carboxamide

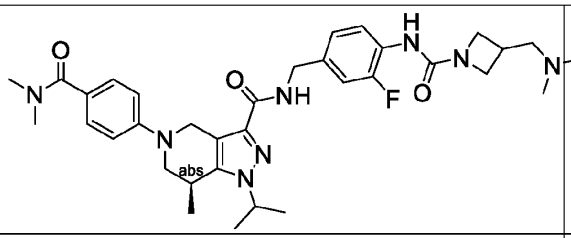
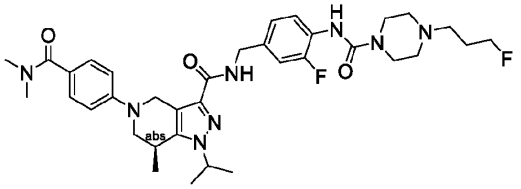
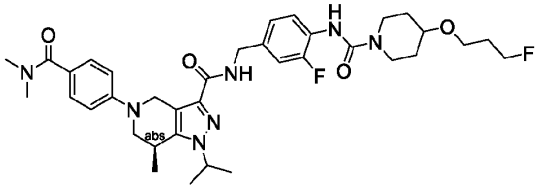
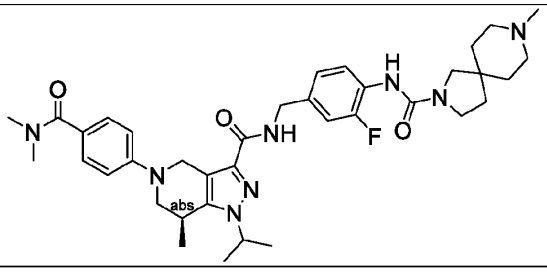
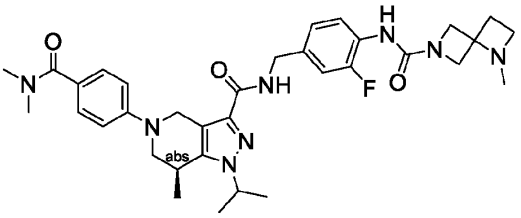
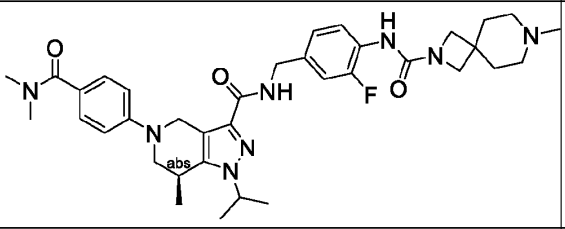
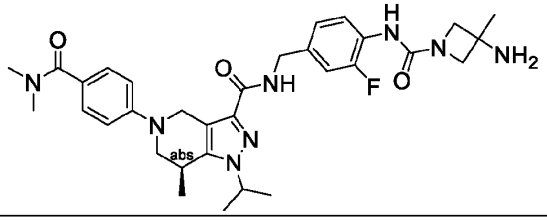
V35		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxo-2-azabicyclo[3.1.0]hexan-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V36		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-methyl-1*H*-1,2,3-triazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V37		*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxo-3-azabicyclo[3.1.1]heptan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V38		*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V39		(*S*)-*N*-(4-(3-amino-3-methylazetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V40		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*RS*)-3,4-dimethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V41		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-methyl-1*H*-pyrazol-1-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

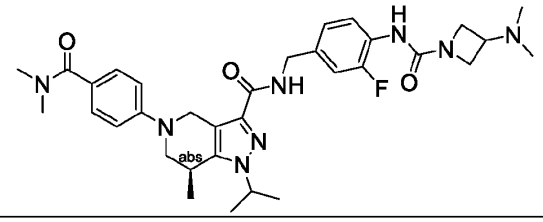
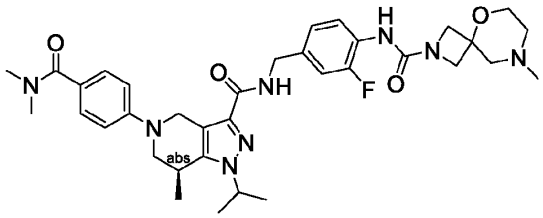
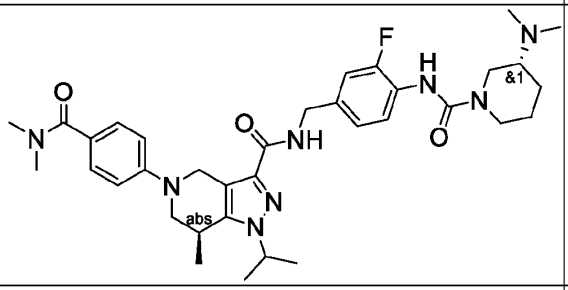
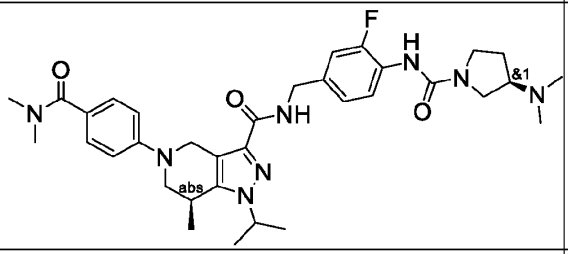
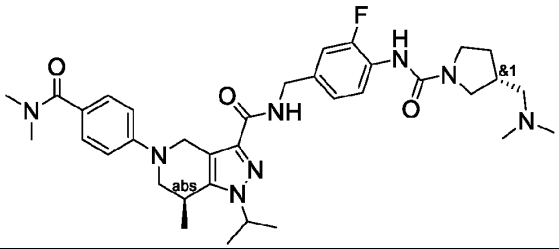
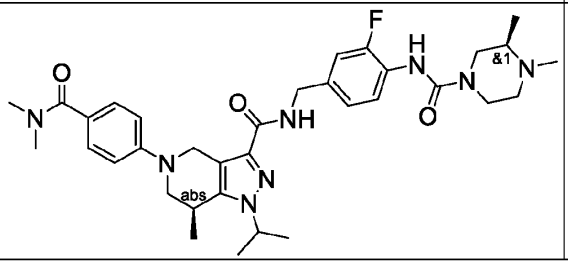
V42		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((*S*)-1-(4-(3,3-dimethylureido)phenyl)ethyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V43		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-((*S*)-1-(4-(4-methylpiperazine-1-carboxamido)phenyl)ethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V44		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(1,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V45		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((1*S*,5*R*)-1-(methylamino)-3-azabicyclo[3.1.0]hexane-3-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V46		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((1*R*,5*S*)-1-(methylamino)-3-azabicyclo[3.1.0]hexane-3-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V47		(*S*)-*N*-(3-fluoro-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-5-(4-(2-oxopyridin-1(2*H*)-yl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V48		(*S*)-5-(4-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)phenyl)-*N*-(3-fluoro-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

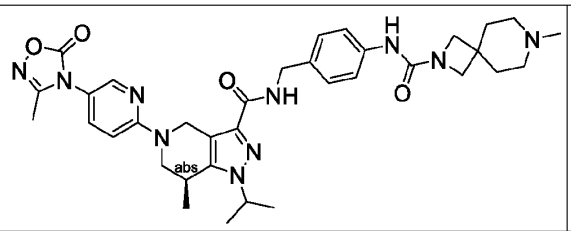
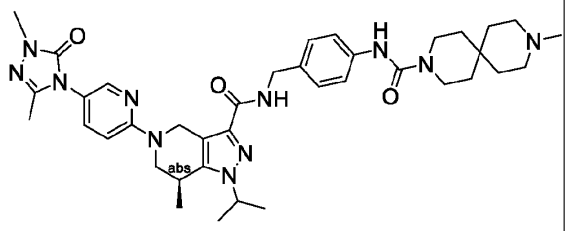
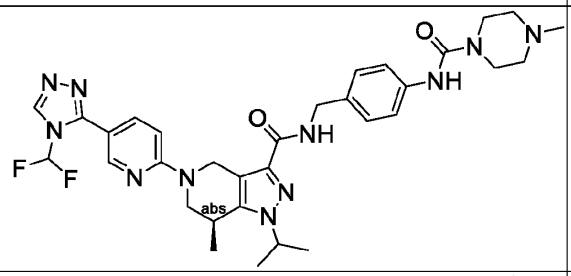
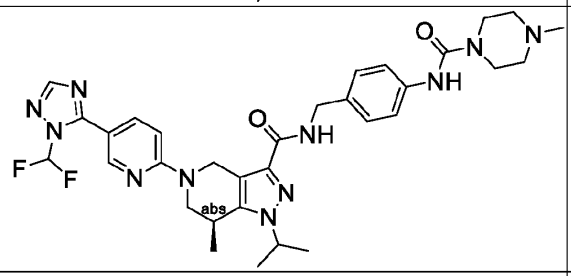
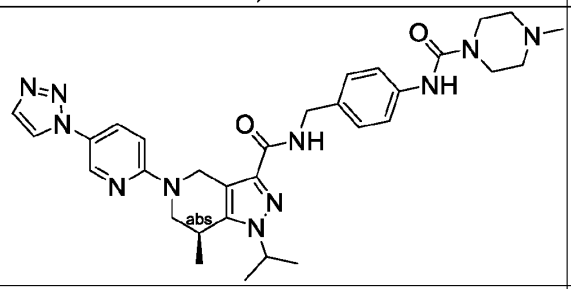
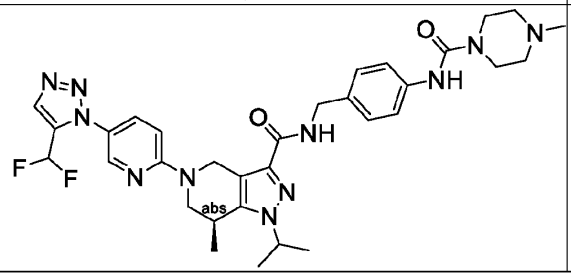
V49		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(3-(2,2,2-trifluoroethyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V50		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methyl-1,6-diazaspiro[3.3]heptane-6-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V51		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V52		(*S*)-*N*-(4-(3-((dimethylamino)methyl)azetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V53		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-8-methyl-2,8-diazaspiro[4.5]decane-2-carboxamide
V54		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(4-(3-fluoropropoxy)piperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V55		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(4-(3-fluoropropyl)piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

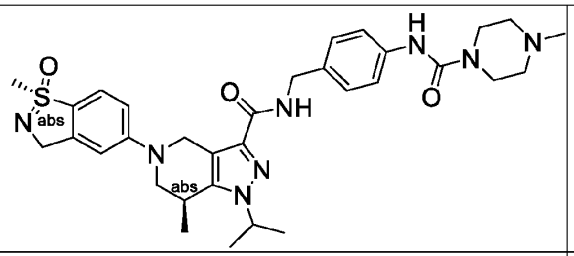
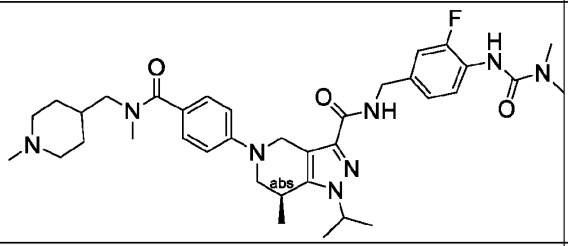
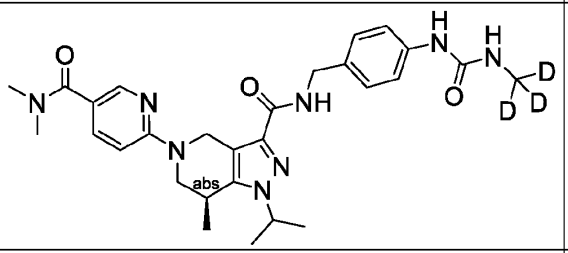
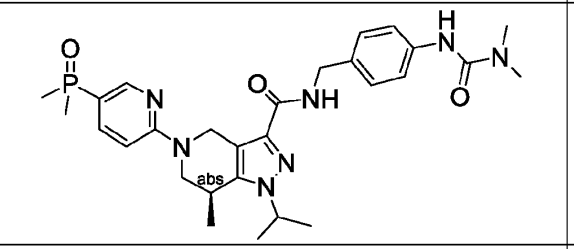
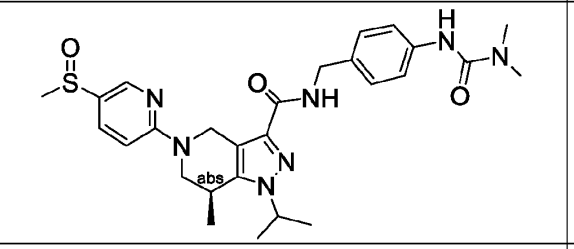
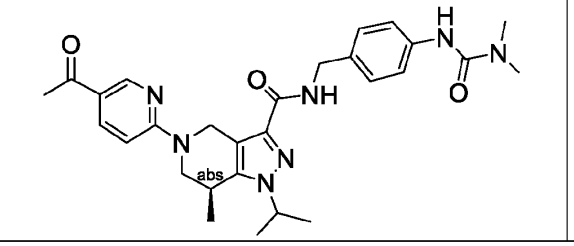
V56		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-8-methyl-5-oxa-2,8-diazaspiro[3.5]nonane-2-carboxamide
V57		(*S*)-*N*-(4-((*RS*)-3-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V58		(*S*)-*N*-(4-((*RS*)-3-(dimethylamino)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V59		(*S*)-*N*-(4-((*RS*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V60		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2,8-diazaspiro[4.5]decane-8-carboxamide
V61		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-5-oxa-2,8-diazaspiro[3.5]nonane-2-carboxamide

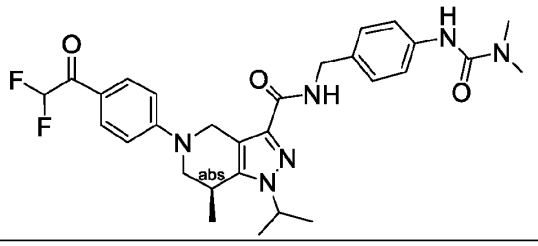
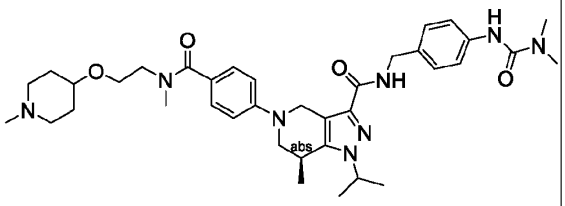
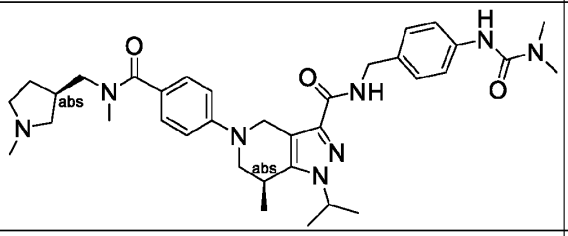
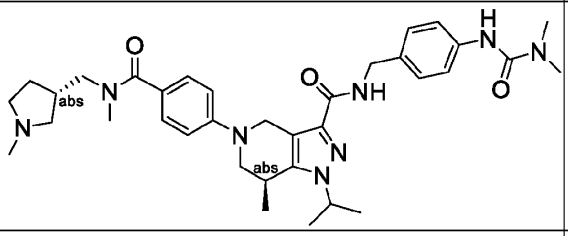
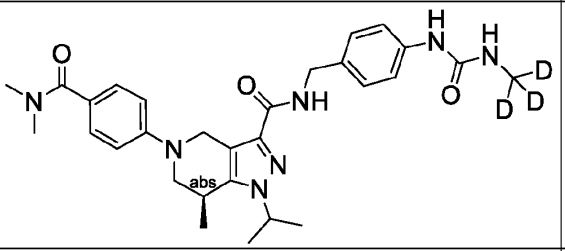
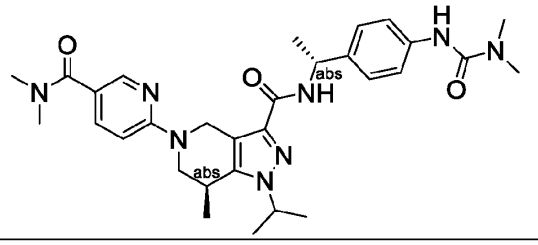
V62		(7*S*)-*N*-(4-(3,8-diazabicyclo[3.2.1]octane-3-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V63		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*RS*)-3-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V64		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((3*RS*,5*SR*)-3,5-dimethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V65		(7*S*)-*N*-(4-(1,6-diazaspiro[3.4]octane-6-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V66		*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-6-oxa-2,9-diazaspiro[4.5]decane-2-carboxamide
V67		*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2,7-diazaspiro[4.5]decane-2-carboxamide
V68		(*S*)-1-isopropyl-7-methyl-5-(5-(4-methyl5-oxo-4,5-dihydro-1,2,4-triazin-3-yl)pyridin-2-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

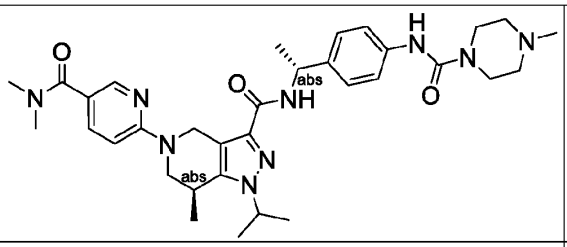
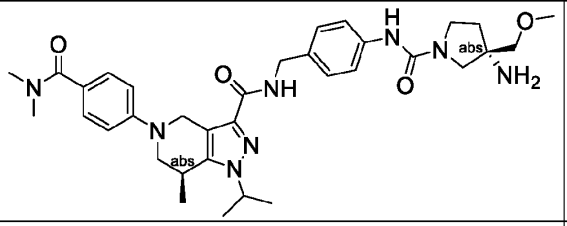
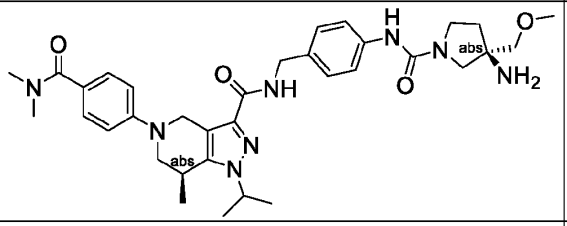
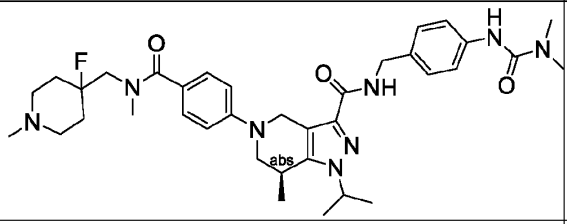
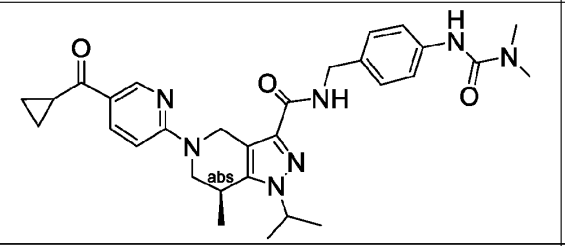
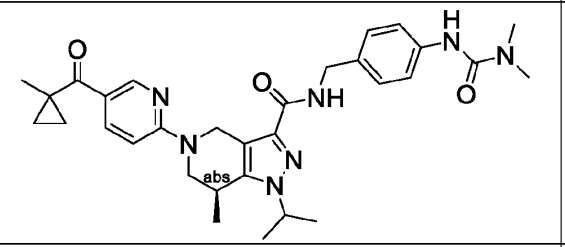
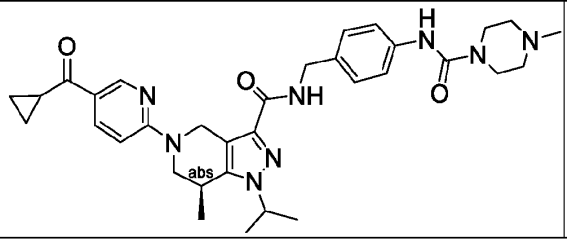
V69		(*S*)-*N*-(4-(3-((dimethylamino)methyl)azetidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V70		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(4-(3-fluoropropyl)piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V71		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(4-(3-fluoropropoxy)piperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V72		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-8-methyl-2,8-diazaspiro[4.5]decane-2-carboxamide
V73		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(1-methyl-1,6-diazaspiro[3.3]heptane-6-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V74		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V75		(*S*)-*N*-(4-(3-amino-3-methylazetidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

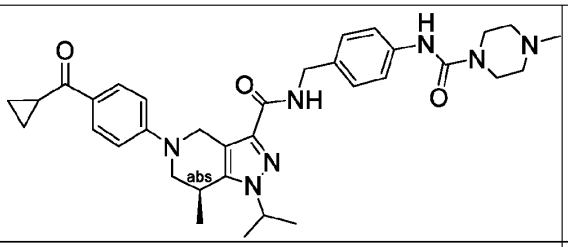
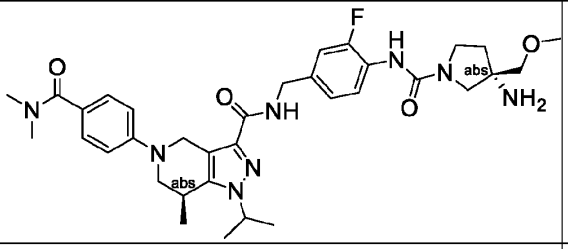
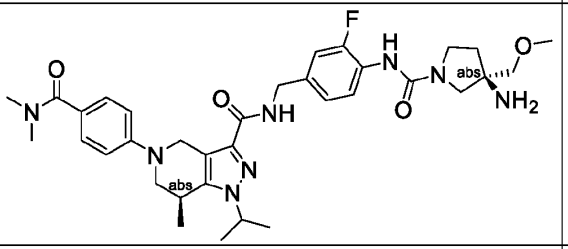
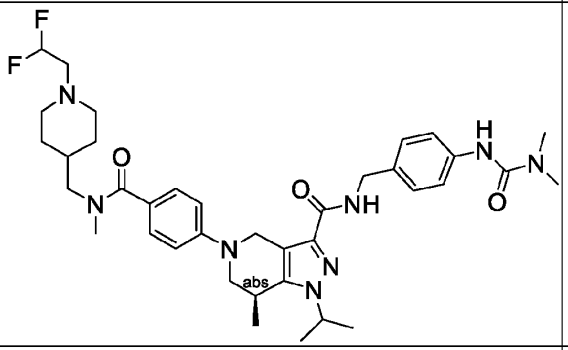
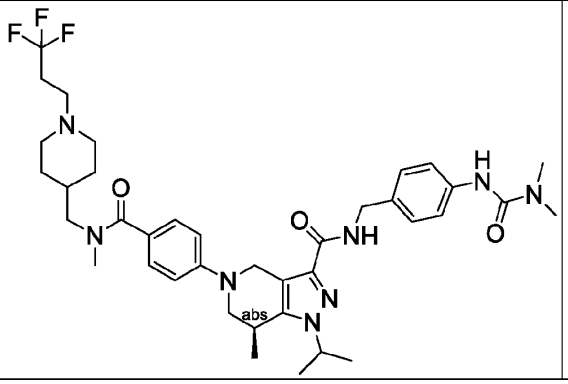
V76		(*S*)-*N*-(4-(3-(dimethylamino)azetidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V77		(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-8-methyl-5-oxa-2,8-diazaspiro[3.5]nonane-2-carboxamide
V78		(*S*)-*N*-(4-((*RS*)-3-(dimethylamino)piperidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V79		(*S*)-*N*-(4-((*RS*)-3-(dimethylamino)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V80		(*S*)-*N*-(4-((*RS*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V81		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*RS*)-3,4-dimethylpiperazine-1-carboxamido)-3-fluorobenzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

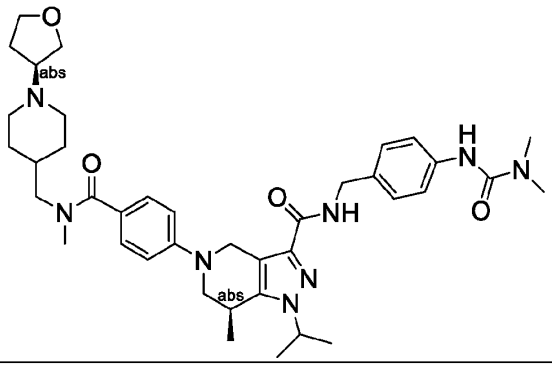
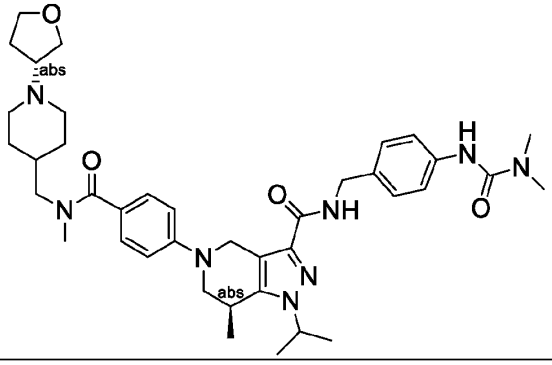
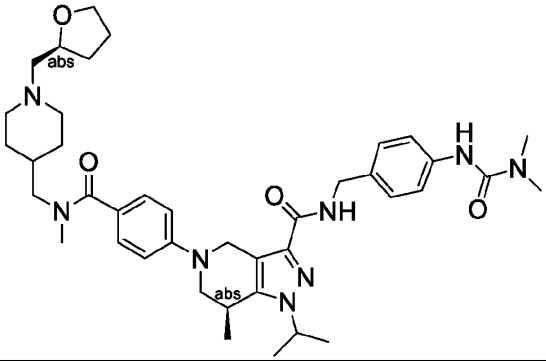
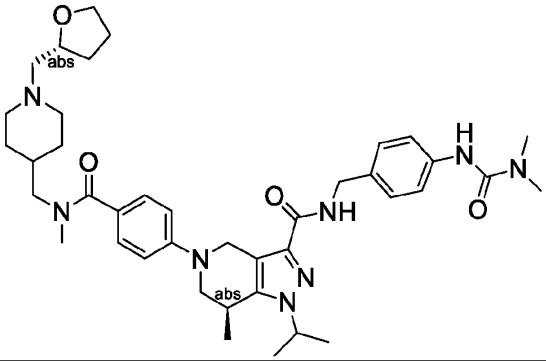
V82		(*S*)-1-isopropyl-7-methyl-*N*-(4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-5-(5-(3-methyl-5-oxo-1,2,4-oxadiazol-4(5*H*)-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V83		(*S*)-*N*-(4-((5-(5-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-9-methyl-3,9-diazaspiro[5.5]undecane-3-carboxamide
V84		(*S*)-5-(5-(4-(difluoromethyl)-4*H*-1,2,4-triazol-3-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V85		(*S*)-5-(5-(1-(difluoromethyl)-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V86		(*S*)-5-(5-(1*H*-1,2,3-triazol-1-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V87		(*S*)-5-(5-(5-(difluoromethyl)-1*H*-1,2,3-triazol-1-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

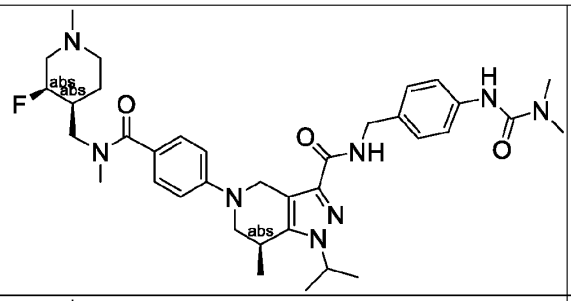
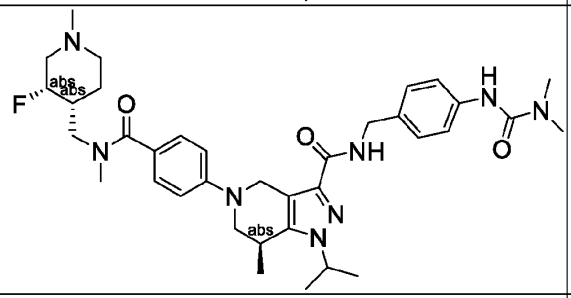
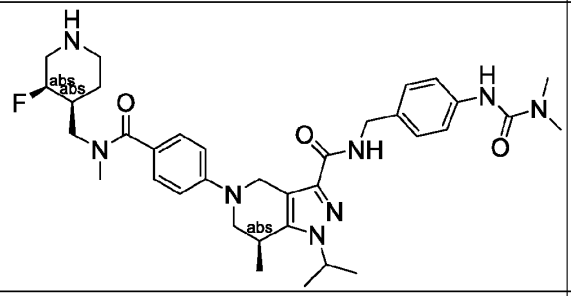
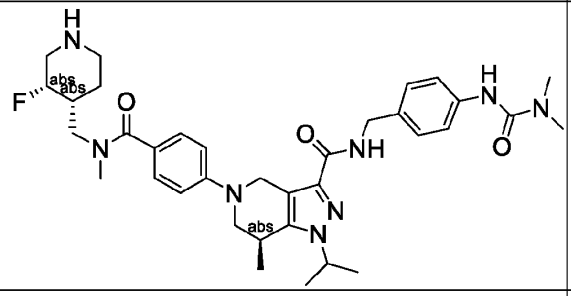
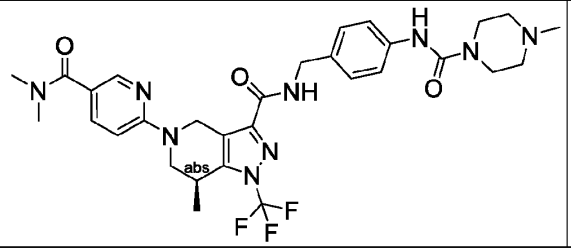
V88		(*S*)-1-isopropyl-7-methyl-5-((*S*)-1-methyl-1-oxido-3*H*-1l4-benzo[*d*]isothiazol-5-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V89		(*S*)-*N*-(4-(3,3-dimethylureido)-3-fluorobenzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-methylpiperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V90		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(3-(methyl-d_3)ureido)benzyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V91		(*S*)-5-(5-(dimethylphosphoryl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V92		(7*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(methylsulfinyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V93		(*S*)-5-(5-acetylpyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

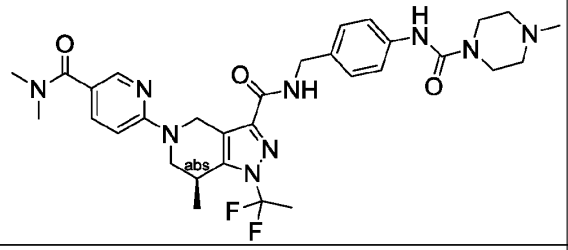
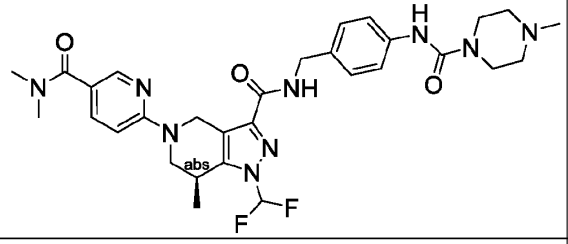
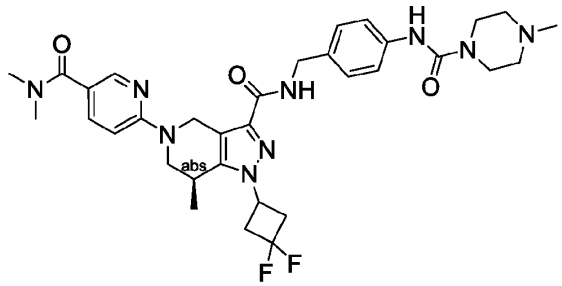
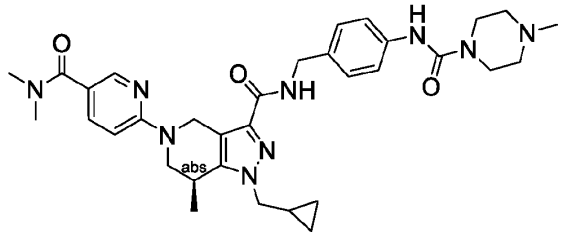
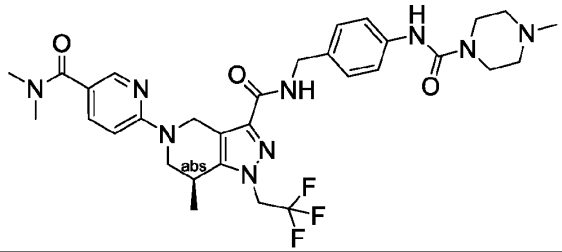
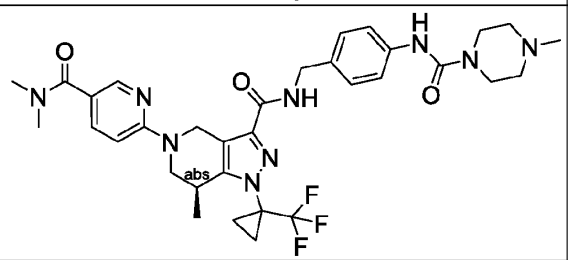
V94		(*S*)-5-(4-(2,2-difluoroacetyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V95		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(2-((1-methylpiperidin-4-yl)oxy)ethyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V96		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(((*R*)-1-methylpyrrolidin-3-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V97		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(((S)-1-methylpyrrolidin-3-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V98		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-(methyl-d_3)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V99		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((*R*)-1-(4-(3,3-dimethylureido)phenyl)ethyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

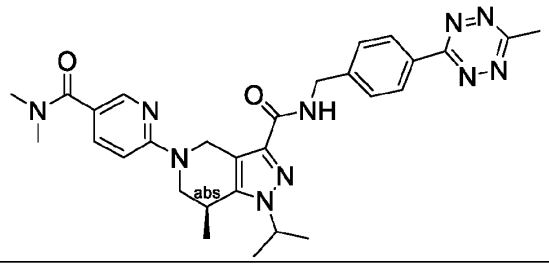
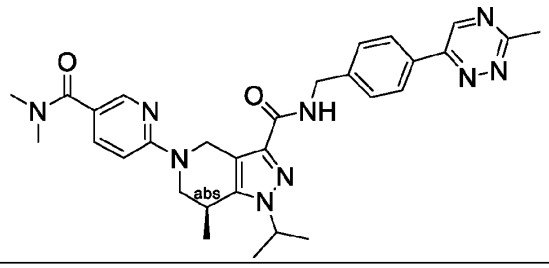
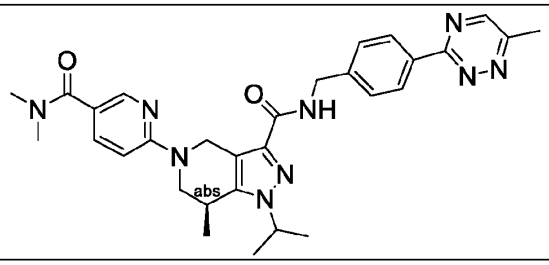
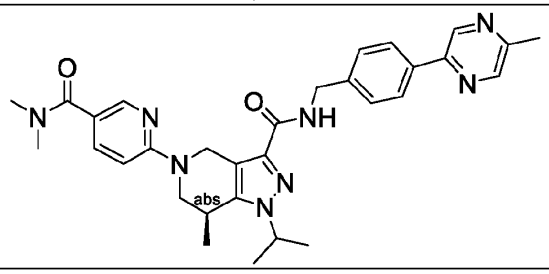
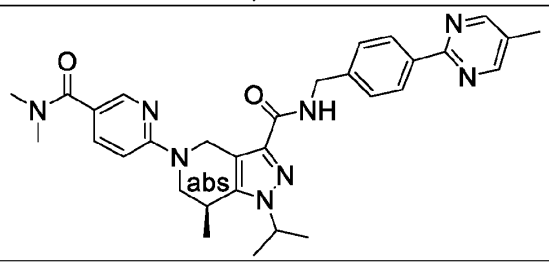
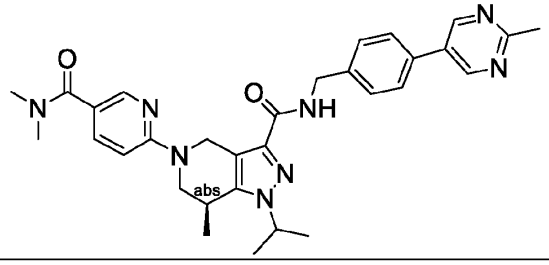
V100		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-((*R*)-1-(4-(4-methylpiperazine-1-carboxamido)phenyl)ethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V101		(*S*)-*N*-(4-((*S*)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V102		(*S*)-*N*-(4-((*R*)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V103		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(4-(((4-fluoro-1-methylpiperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V104		(*S*)-5-(5-(cyclopropanecarbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V105		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(1-methylcyclopropane-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V106		(*S*)-5-(5-(cyclopropanecarbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

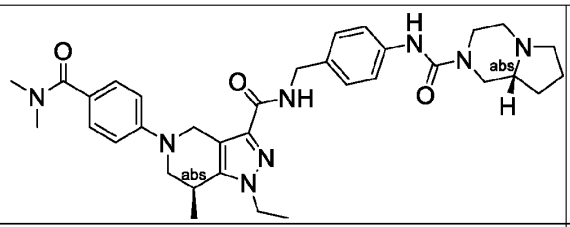
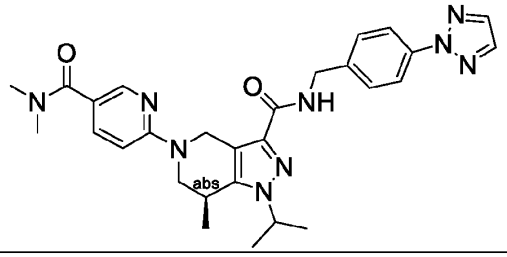
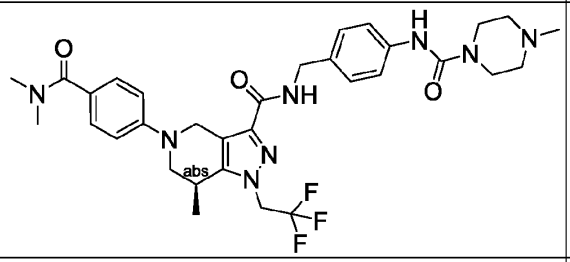
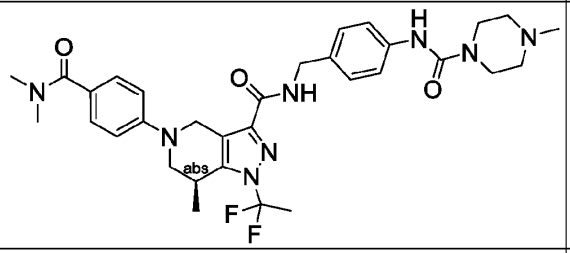
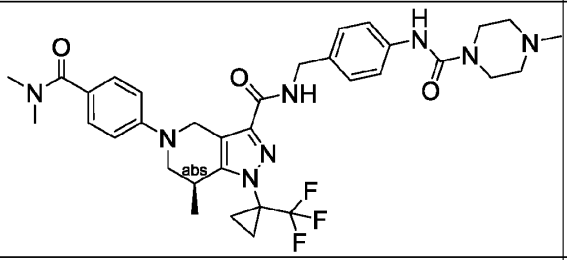
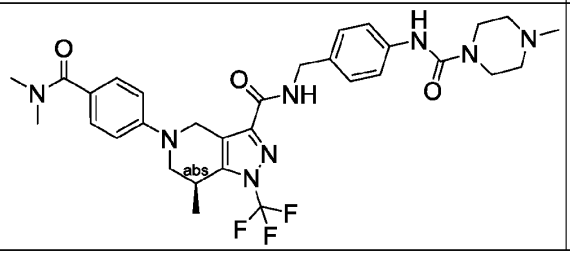
V107		(*S*)-5-(4-(cyclopropanecarbonyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V108		(*S*)-*N*-(4-((*S*)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V109		(*S*)-*N*-(4-((*R*)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V110		(*S*)-5-(4-(((1-(2,2-difluoroethyl)piperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V111		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-(3,3,3-trifluoropropyl)piperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

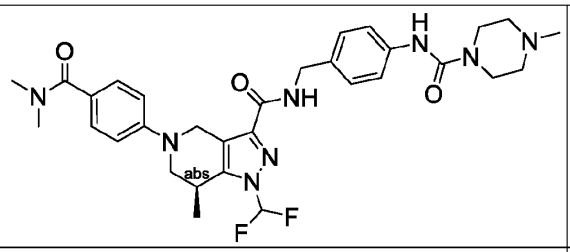
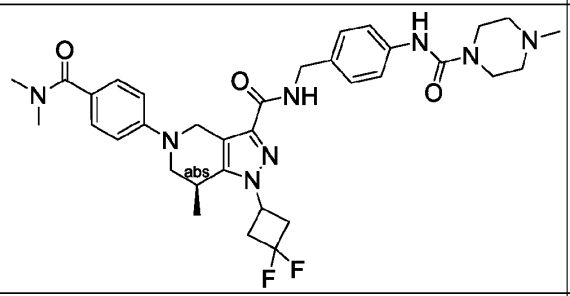
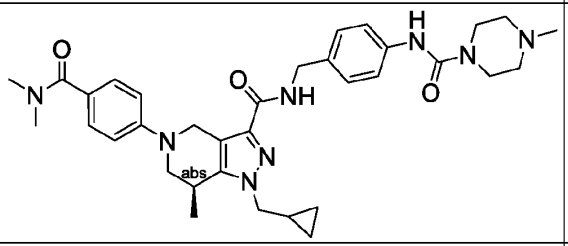
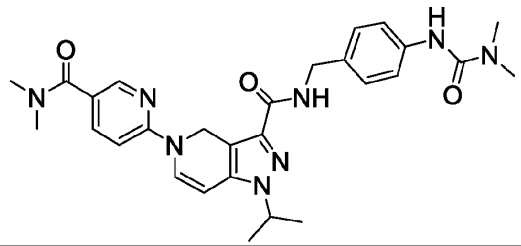
V112		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-((*S*)-tetrahydrofuran-3-yl)piperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V113		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-((*R*)-tetrahydrofuran-3-yl)piperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V114		*(S)*-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-(((*S*)-tetrahydrofuran-2-yl)methyl)piperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V115		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-(((*R*)-tetrahydrofuran-2-yl)methyl)piperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

V116		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(4-((((3*R*,4*S*)-3-fluoro-1-methylpiperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V117		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(4-((((3*S*,4*R*)-3-fluoro-1-methylpiperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V118		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(4-((((3*R*,4*S*)-3-fluoropiperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V119		(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(4-((((3*S*,4*R*)-3-fluoropiperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V120		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-1-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

V121		(*S*)-1-(1,1-difluoroethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V122		(*S*)-1-(difluoromethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V123		(*S*)-1-(3,3-difluorocyclobutyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V124		(*S*)-1-(cyclopropylmethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V125		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V126		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-1-(1-(trifluoromethyl)cyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

V127		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(6-methyl-1,2,4,5-tetrazin-3-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V128		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(3-methyl-1,2,4-triazin-6-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V129		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(6-methyl-1,2,4-triazin-3-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V130		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(5-methylpyrazin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V131		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(5-methylpyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V132		(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(2-methylpyrimidin-5-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

V133		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-ethyl-7-methyl-*N*-(4-((*R*)-octahydropyrrolo[1,2-a]pyrazine-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V134		(*S*)-*N*-(4-(2*H*-1,2,3-triazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V135		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V136		(*S*)-1-(1,1-difluoroethyl)-5-(4-(dimethylcarbamoyl)phenyl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V137		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-1-(1-(trifluoromethyl)cyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V138		(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-1-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

V139		(*S*)-1-(difluoromethyl)-5-(4-(dimethylcarbamoyl)phenyl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V140		(*S*)-1-(3,3-difluorocyclobutyl)-5-(4-(dimethylcarbamoyl)phenyl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V141		(*S*)-1-(cyclopropylmethyl)-5-(4-(dimethylcarbamoyl)phenyl)-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
V142		5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5-dihydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

Pharmacology Assays

STAT6 Reporter Luciferase Assay

Pharmacological measurements of STAT6 transcriptional activity through the IL-13-IL-13 receptor/IL-4 receptor pathway were made with a stably transfected HaCaT keratinocyte cell line, which expresses NanoLuc luciferase reporter gene under the transcriptional control of the STAT6 responsive promoter for IL-13Ra2. The readout of the STAT6 activity utilized Promega Nano-Glo Luciferase assay kit.

The reporter cells were cultured in a growth media comprised of DMEM High Glucose, no calcium and no glutamine, 10% heat inactivated fetal bovine serum (HI FBS), 1% 100x Glutamax, and 100 U/mL Penicillin-Streptomycin (units of penicillin in 1 mL of streptomycin). Seven thousand cells were plated in 25 microliter (µL) per well in a 384-well, white bottom, tissue culture plate. Cells were cultured overnight at 37 ºC. The next day, test compounds (solubilized and serially diluted in DMSO, in an 11 point, 4-fold dilution series in duplicate) were

spotted, 60 nanoliters (nL) per well, into a 384 well v-bottom polypropylene plate. Thirty µL per well of 37 ºC dosing media (Dulbecco's modified eagle medium (DMEM) High Glucose, no calcium and no glutamine with 2% HI FBS) was added to the compound plate. Growth media was removed from the cell plate, and the cells were washed with DPBS. Twenty µL per well of compounds diluted in dosing media were transferred from the compound plate to the cell plate and the compounds were further diluted with an additional 15 µL of dosing media in the cell plate: the cell plate was incubated for two hours at 37 ºC. After two hours, STAT6 activity was stimulated with the addition of 5 µL per well of IL-13 (R&D Systems) in dosing media with a final concentration of 0.12 nM IL13. Cells were incubated at 37 ºC for 4 hours to allow for reporter gene expression, then all media was removed from the plate. The cell plates were treated with assay buffer and Luciferase substrate from Nano-Glo Luciferase Assay Kit for 15 min and then measured for luminescence on an EnVision 2105 multilabel reader (PerkinElmer). EC_{50} (half maximal effective concentration) values were determined from this data using a 4-parameter fit algorithm and are provided in Table 2, where the EC_{50} values are the statistical mean values of n number of samples as denoted by n(EC_{50}).

Human Whole Blood (HWB) CCL17 TR-FRET Assay

The IC_{50} (half-maximal concentration required for inhibition) of compounds for the inhibition of CCL17 secretion in peripheral human whole blood, stimulated through the IL-13-IL-13 receptor/IL-4 receptor pathway was evaluated with a TR-FRET sandwich ELISA CCL17 (TARC) Assay Kit (Bioauxilium).

Test compounds (solubilized and serially diluted in DMSO, in an 11 point, 3-fold dilution series in duplicate) were spotted, 80 nL per well, into a 384 well v-bottom polypropylene plate. Human whole blood was collected from a peripheral vein, 714 units of sodium heparin was added for every 50 mL of blood collected. Sixty µL per well of blood was added to the compound plate. The blood plate was incubated for two hours at 37 °C. After two hours, CCL17 production was stimulated with the addition of 20 µL per well of IL13 (R&D Systems) in HBSS with calcium and magnesium, with a final concentration of 10 ng/mL IL13. The plate containing blood, compound, and IL-13 was incubated at 37 °C for 48 hours, to allow for CCL17 production. After 48 hours, the plate was centrifuged at 1,500 revolutions per minute (RPM) for 7 minutes, with no braking. The CCL17 TR-FRET Assay Kit detection reagent was prepared according to kit instructions and 4 µL per well of the antibody cocktail was added to a 384-well white low volume non-binding coated plate (Corning). Sixteen µL of serum from the centrifuged blood plate was transferred to the detection plate containing the TR-FRET antibody cocktail. The plate was centrifuged briefly, then covered and incubated 16 hours at room temperature. The plate was then read on an EnVision 2105 multilabel reader (PerkinElmer) with settings for TR-FRET Ratio = 10,000 X (fluorescence intensity 665 nm / fluorescence intensity 615 nm). IC_{50} values were determined from this data using a 4-parameter fit algorithm and are shown in

Table 3, where the EC_{50} values are the statistical mean values of n number of samples as denoted by n(IC_{50}).

Table 3					
Ex.	Reporter EC_{50} (μM)	n (EC_{50})	HWB CCL17 IC_{50} (μM)	n (IC_{50})	ChemDraw Name
1	0.011	2	0.318	6	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
2	0.008	72	0.069	172	5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
3	0.010	6	0.104	10	5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
4	0.178	2	1.108	2	5-(4-(Dimethylcarbamoyl)phenyl)-1-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
5	0.124	2	0.927	7	7-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
6	0.004	32	0.025	72	*rac*-(*R*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
7	0.033	5	0.196	6	*rel*-(*R or S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
8	0.003	4	0.014	6	*rel*-(*R or S*)-5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
9	0.015	2	0.027	3	*rac*-(*R*)-7-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide formate
10	0.011	2	0.094	6	1-cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
11	0.016	3	0.205	2	*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

12	0.016	2	0.093	3	*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
13	0.017	2	0.083	7	3-cyclopropyl-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
14	0.029	4	0.260	7	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
15	0.159	2	1.162	6	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
16	0.261	2	0.791	2	3-cyclopropyl-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(methylcarbamoyl)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
17	0.322	2	0.291	3	7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
18	1.421	2	1.379	5	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
19	> 10.000	1	3.364	2	2-cyclopropyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
20	0.006	2	0.072	3	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
21	0.033	4	0.217	4	*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
22	0.021	2	0.054	2	7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
23	0.006	2	0.062	2	*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxamide
24	0.384	2	0.346	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-*a*]pyrazine-3-carboxamide

25	0.164	2	1.487	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine-3-carboxamide
26	0.069	2	0.561	2	*rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7-tetrahydro-1*H*-indazole-3-carboxamide
27	0.006	2	0.091	2	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
28	0.046	2	0.313	5	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydroisoxazolo[4,5-*c*]pyridine-3-carboxamide
29	2.230	2	0.878	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-3-carboxamide
30	0.005	2	0.087	5	*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
31	0.007	4	0.085	7	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
32	0.009	2	0.040	2	7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
33	0.002	2	0.035	3	5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
34	0.008	2	0.071	3	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
35	0.009	2	0.047	3	5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
36	0.024	3	0.254	7	*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
37	0.030	2	0.701	6	5-(1-acetyl-1,2,3,4-tetrahydroquinolin-6-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

38	0.072	2	1.636	3	*N*-(4-(1*H*-imidazol-2-yl)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxamide
39	0.748	2	>30.000	1	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
40	0.038	2	0.324	2	*N*-(4-(4H-1,2,4-triazol-3-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
41	0.003	2	0.093	3	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
42	0.010	2	0.136	2	*N*-(4-(3,3-dimethylureido)benzyl)-7-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-3-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
43	0.286	2	1.305	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(6-oxo-1,6-dihydropyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
44	0.503	2	5.402	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(6-oxo-1,6-dihydropyridin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
45	0.004	2	0.050	2	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
46	0.009	2	0.110	3	1-cyclopropyl-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
47	1.177	2	> 30.000	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-1*H*-pyrazol-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
48	0.952	2	3.957	5	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine-3-carboxamide
49	0.009	2	0.039	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
50	0.035	2	0.151	1	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

51	0.004	2	0.030	2	*(S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
52	0.009	2	0.064	2	3-(1,1-difluoroethyl)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
53	0.008	2	0.019	3	*rel-(R* or *S)*-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
54	0.120	2	0.332	3	*rel-(R* or *S)*-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3,5-dimethyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
55	0.010	3	0.012	1	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,4-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
56	0.013	2	0.369	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-5-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
57	0.098	2	0.182	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
58	0.024	2	0.170	3	*rel-(R or S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
59	0.003	2	0.027	3	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
60	0.032	2	0.910	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
61	0.075	2	2.586	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
62	0.009	2	0.066	2	*rac*-(*R*)-1-(1-cyclopropylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
63	0.014	2	0.105	2	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

64	0.004	2	0.073	2	5-(5-(1*H*-1,2,3-triazol-1-yl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
65	0.208	2	28.130	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-oxo-5-azaspiro[2.4]heptan-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
66	0.013	2	0.089	1	*(S)*-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methyl-2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
67	0.064	2	5.021	1	*(R)*-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methyl-2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
68	0.009	2	0.043	2	*rac*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxamide
69	1.074	2	8.108	1	(*S*)-N-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-(hydroxymethyl)-5-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
70	0.008	2	0.081	3	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7,7-difluoro-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
71	0.002	2	0.014	3	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
72	0.308	2	1.104	3	*rac*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-1,4,5,7,8,9-hexahydro-4,8-epiminooxocino[5,4-*c*]pyrazole-3-carboxamide
73	0.121	2	9.348	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-oxo-4-azaspiro[2.4]heptan-4-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
74	0.011	2	0.120	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-propyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
75	2.829	2	4.558	1	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-(hydroxymethyl)-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

76	0.057	2	0.156	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
77	0.004	2	0.045	3	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-c]pyridine-3-carboxamide
78	0.003	2	0.014	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
79	0.041	2	1.778	1	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-ethyl-5-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
80	> 10.000	1	> 30.000	1	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(5-(hydroxymethyl)-2-oxooxazolidin-3-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
81	0.034	2	0.115	3	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(1-(4-(3,3-dimethylureido)phenyl)ethyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
82	0.101	2	0.112	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
83	0.086	2	0.278	2	*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
84	0.002	2	0.056	1	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-fluoro-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
85	0.006	2	0.090	3	*rac*-(*R*)-1-(*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
86	> 10.000	1	> 30.000	1	*rac*-(4*R*,7*S*)-9-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-1,4,5,6,7,8-hexahydro-4,7-epiminocyclohepta[*c*]pyrazole-3-carboxamide
87	0.015	2	0.118	1	*rel*-(*R or S*)-1-(1-cyclopropylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

88	0.424	2	2.078	1	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-(hydroxymethyl)-5-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
89	0.012	2	0.149	2	1-(cyclopropylmethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
90	0.025	2	0.067	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydrofuran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
91	0.014	2	0.327	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
92	0.020	2	0.062	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-methoxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
93	0.525	2	2.270	1	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-hydroxy-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
94	0.049	2	0.089	3	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(oxetan-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
95	0.001	2	0.006	6	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
96	0.005	2	0.066	3	1-cyclobutyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
97	0.065	2	3.483	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-5-azaspiro[2.4]heptan-5-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
98	0.048	2	0.573	1	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-fluoro-2-oxopyrrolidin-1-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
99	0.017	2	0.453	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methyl-2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
100	0.174	2	1.796	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-oxo-1,4-oxazepan-4-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

101	0.005	2	0.053	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
103	0.047	2	0.535	1	N-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxomorpholino)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
104	0.007	2	0.107	3	1-(bicyclo[1.1.1]pentan-1-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
105	0.003	2	0.021	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-N-(4-(3,3-dimethylureido)benzyl)-1,7,7-trimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
106	0.008	2	0.049	1	5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-methyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide
107	0.013	2	0.219	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
108	0.030	2	0.536	4	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
109	0.117	2	> 30.000	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxo-2-azabicyclo[2.2.1]heptan-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
110	0.523	2	2.089	1	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-(hydroxymethyl)-2-oxooxazolidin-3-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
111	0.003	4	0.013	4	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
112	0.015	2	0.078	4	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
113	0.017	3	0.161	4	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
114	0.020	3	0.211	4	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

115	0.002	2	0.012	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
116	0.010	2	0.061	1	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
117	0.003	2	0.013	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
118	0.025	2	0.116	1	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
119	0.0003	2	0.004	4	(*S*)-1-cyclobutyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
120	0.001	2	0.004	4	(*S*)-1-(cyclopropylmethyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
121	0.001	2	0.006	5	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
122	0.024	2	0.900	4	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
123	0.041	2	1.012	3	*rel*-(*R* or *S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
124	0.0003	2	0.005	5	*rel*-(*R* or *S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
125	0.001	4	0.004	4	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
126	0.001	3	0.005	4	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

127	0.001	5	0.004	4	(*S*)-5-(5-dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
128	0.0003	5	0.003	8	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
129	0.001	2	0.009	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
130	0.023	2	0.077	3	*rac*-(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5-ethyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
131	0.103	2	0.256	3	*rel*-(*R* or *S*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5-ethyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
132	0.0002	2	0.0036	3	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-N-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-c]pyridine-3-carboxamide
133	0.028	2	0.048	3	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
134	0.007	2	0.046	3	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
135	0.136	2	1.268	2	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(methylcarbamoyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
136	0.012	4	0.196	3	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
137	1.864	2	9.688	2	5-(5-carbamoylpyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
138	0.248	2	1.137	3	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(methylsulfonamido)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
139	0.002	5	0.007	6	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

140	0.012	2	0.144	1	*N*-(4-((3*R*,4*S*)-3,4-difluoropyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
141	0.022	2	0.078	1	*N*-(4-(3-(dimethylamino)azetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
142	0.015	2	0.039	1	(1*S*,4*S*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-oxa-5-azabicyclo[2.2.2]octane-5-carboxamide
143	0.011	2	ND	ND	*rac*-*N*-(4-((1*R*,4*S*)-2-azabicyclo[2.2.1]heptane-2-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-*c*]pyridine-3-carboxamide
144	0.007	2	0.292	1	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
145	0.006	2	ND	ND	*rac*-(*R*)-*N*-(4-(3-(difluoromethyl)pyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
146	0.127	2	2.116	3	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(1,1-dioxidoisothiazolidin-2-yl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
147	0.026	2	0.252	3	*N*-(4-acetamidobenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
148	0.010	2	0.176	3	1-(*tert*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
149	0.005	1	ND	ND	*N*-(4-(4-(cyanomethyl)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
150	0.018	2	0.070	2	*N*-(4-(3-(dimethylamino)-3-methylazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

151	0.009	1	ND	ND	*N*-(4-(3-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
152	0.031	2	0.155	2	*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-oxa-6-azaspiro[3.4]octane-6-carboxamide
153	0.011	2	0.108	1	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-fluoropyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
154	0.008	2	0.449	2	*N*-(4-(3-(cyclopropylmethyl)ureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
155	0.012	2	0.141	1	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-((tetrahydrofuran-3-yl)methyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
156	0.006	2	0.058	1	*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-oxa-7-azaspiro[3.5]nonane-7-carboxamide
157	0.008	2	0.535	2	*N*-(4-(3-cyclobutylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
158	0.015	2	0.130	1	*N*-(4-(3-cyanoazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
159	0.016	2	0.059	1	(*S*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-(hydroxymethyl)morpholine-4-carboxamide
160	0.015	2	0.021	1	*rac-(R)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-hydroxy-3-methylpyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
161	0.007	2	0.199	2	*N*-(4-(4-(difluoromethyl)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
162	0.011	2	0.066	1	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(4-(2-hydroxyethoxy)piperidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

163	0.016	2	0.030	1	*N*-(4-(3-amino-3-methylazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
164	0.013	2	0.045	1	*rac*-(*R*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-6-oxa-2,9-diazaspiro[4.5]decane-2-carboxamide
165	0.014	2	0.156	1	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methoxy-3-methylazetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
166	0.004	2	0.021	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-((3*S*,4*S*)-3-hydroxy-4-methoxypyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
167	0.029	2	0.154	2	(*R*)-*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-(hydroxymethyl)morpholine-4-carboxamide
168	0.024	3	0.111	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methyl-3-(oxetan-3-ylmethyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
169	0.032	3	0.125	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-((1*s*,3*s*)-3-hydroxycyclobutyl)ureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
170	0.017	2	0.082	1	(*S*)-*N*-(4-(3-(dimethylamino)pyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
171	0.005	2	0.057	2	*rac*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-((3*R*,4*R*)-3-fluoro-4-methoxypyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
172	0.011	2	0.150	1	*N*-(4-(4-cyano-4-methylpiperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
173	0.011	2	0.072	1	*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)morpholine-4-carboxamide

174	0.040	2	0.212	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(2-(hydroxymethyl)pyrrolidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
175	0.007	2	0.067	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(4-(hydroxymethyl)piperidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
176	0.012	2	0.051	2	*rac*-(*R*)-*N*-(4-(3-((1,4-dioxan-2-yl)methyl)-3-methylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
177	0.008	2	0.051	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
178	0.007	2	0.045	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-(2-methoxyethyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
179	0.007	2	0.064	2	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methoxypyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
180	0.018	2	0.055	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-(2-hydroxyethyl)-3-methylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
181	0.260	2	0.436	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-(oxetan-3-ylmethyl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
182	0.017	2	0.131	2	(*S*)-*N*-(4-(3-cyanopyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
183	0.016	2	0.067	1	(*R*)-*N*-(4-(3-cyanopyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
184	0.027	2	0.092	2	*N*-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-6-oxa-3-azabicyclo[3.1.1]heptane-3-carboxamide
185	0.024	2	0.083	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-hydroxy-3-methylazetidine-1-carboxamido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

186	0.010	2	ND	ND	*N*-(4-(3-azabicyclo[3.1.0]hexane-3-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
187	0.015	2	0.041	1	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methyl-3-(tetrahydrofuran-3-yl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
188	0.011	2	0.069	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(3-methoxyazetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
189	0.010	2	0.095	1	*N*-(4-(3-(2,2-difluoroethyl)-3-methylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
190^	0.020	2	0.038	1	*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydrofuran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
191^	0.032	2	0.126	3	*rel-(R* or *S)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydrofuran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
192	1.674	2	6.445	3	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(6-methoxy-5-(3-methyl-2-oxopiperidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
193	0.372	3	ND	ND	(*S*)-5-(5-(3-acetamidopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
194	0.401	2	ND	ND	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-(methoxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
195	0.164	3	ND	ND	5-(5-(1,4-oxazepane-4-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
196	0.090	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-propionylpiperazine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
197	0.197	3	ND	ND	(*S*)-5-(5-(2-carbamoylpyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

198	0.210	2	ND	ND	*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxypyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
199	0.125	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methoxypiperidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
200	0.363	3	ND	ND	5-(5-(4-acetyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
201	0.343	3	ND	ND	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-ethoxypyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
202	8.077	1	ND	ND	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(6-methoxy-5-(3-methyl-5-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
203^	0.001	2	0.016	2	*rel-(R* or *S)-N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
204^	0.016	2	0.246	2	*rel-(R* or *S)-N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
205	0.005	2	0.019	2	*rac*-(*R*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
206	0.097	1	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(morpholine-4-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
207	0.272	3	ND	ND	5-(5-((2*R*,6*S*)-2,6-dimethylmorpholine-4-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
208	0.535	3	ND	ND	*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(2-(hydroxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carbo*xamide*
209	0.692	3	ND	ND	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methoxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

210	1.063	3	ND	ND	5-(5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
211	0.934	3	ND	ND	(*R*)-5-(5-(3-acetamidopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
212	0.278	3	ND	ND	5-(5-((1*R*,5*S*)-6-oxa-3-azabicyclo[3.1.1]heptane-3-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
213	0.718	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(ethyl(2-(methylamino)-2-oxoethyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
214	0.502	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5-oxo-1,4-diazepane-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
215	0.276	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
216	0.546	3	ND	ND	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methoxypyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
217	0.272	3	ND	ND	5-(5-(2,2-dimethyl-3-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
218	2.380	3	ND	ND	(*R*)-5-(5-(2-carbamoylpyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
219	1.314	3	ND	ND	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxy-3-methylpyrrolidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
220	0.336	3	ND	ND	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxypiperidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
221	0.227	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxo-1,4-diazepane-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

222	1.478	3	ND	ND	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methylcarbamoyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
223	0.201	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-oxopiperazine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
224	0.163	3	ND	ND	5-(5-(4-acetylpiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
225	0.644	3	ND	ND	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methoxymethyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
226	1.932	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methoxy-3-methylazetidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
227	> 6.116	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-((1*S*,4*S*)-6-oxo-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
228	0.116	3	ND	ND	5-(5-(2-oxa-6-azaspiro[3.4]octane-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
229	0.592	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((2-(ethylamino)-2-oxoethyl)(methyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
230^	0.014	2	0.277	3	*rel*-(5*aR*,7*aS*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,5a,6,7,7a-hexahydro-1*H*-cyclobuta[*b*]pyrazolo[3,4-*d*]pyridine-3-carboxamide
231^	0.002	2	0.023	2	*rel*-(5*aR*,7*aS*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4,5,5a,6,7,7a-hexahydro-1*H*-cyclobuta[*b*]pyrazolo[3,4-*d*]pyridine-3-carboxamide
232^	0.002	2	0.005	2	*rel*-(*R* or *S*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide

233^	0.042	2	0.078	2	*rel-(R* or *S*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
234^	0.020	2	0.080	1	*rel-(R* or *S*)-1-(*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
235^	0.015	2	0.085	1	*rel-(R* or *S*)-1-(*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
236	0.017	2	0.254	1	ethyl (4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate
237^	0.007	2	0.083	1	*rel-(R* or *S*)-1-(1-cyclopropylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
238	0.002	2	0.009	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
239	0.236	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4*aR*,7*aS*)-hexahydro-5*H*-[1,4]dioxino[2,3-*c*]pyrrole-6-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
240	3.632	2	ND	ND	5-(5-(3-cyano-3-methylpyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
241	0.330	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((3*aS*,6*aS*)-hexahydro-2*H*-furo[2,3-*c*]pyrrole-5-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
242	0.352	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-ethoxyazetidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
243	1.652	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(6-hydroxy-3-azabicyclo[3.1.1]heptane-3-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
244	0.196	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(3-hydroxy-3-methylazetidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

245	2.092	3	ND	ND	*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methylcarbamoyl)pyrrolidine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
246	0.001	2	0.010	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
247	0.001	2	0.009	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
248	0.035	2	0.131	2	1-((3,3-difluorocyclobutyl)methyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
249	0.006	2	0.031	1	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
250^	0.002	2	0.028	2	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
251^	0.010	2	0.080	2	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
252	0.385	2	1.131	2	6-(10-(4-(3,3-dimethylureido)benzyl)-11-oxo-1,3,4,7,8,9,10,11-octahydro-2*H*-pyrido[4',3':3,4]pyrazolo[1,5-*a*][1,4]diazepin-2-yl)-*N,N*-dimethylnicotinamide
253	0.007	2	0.126	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-neopentyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
254	0.022	2	0.180	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(tetrahydro-2*H*-pyran-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
255	0.003	2	0.048	3	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
256	0.028	2	0.190	2	6-(9-(4-(3,3-dimethylureido)benzyl)-10-oxo-3,4,7,8,9,10-hexahydropyrido[4',3':3,4]pyrazolo[1,5-*a*]pyrazin-2(1*H*)-yl)-*N,N*-dimethylnicotinamide

257	0.015	2	0.272	2	1-(cyclobutylmethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
258^	0.002	2	0.008	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
259	0.002	2	0.030	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,6-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
260	0.010	2	0.064	4	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
261	3.573	2	> 30.0	1	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(*tert*-pentyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
262^	0.001	2	0.006	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-((*RS*)-1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
263	0.009	2	0.130	3	1-(1-cyclobutylethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
264	0.007	2	0.131	4	1-cyclopentyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
265	0.005	2	0.037	3	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-isopropyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
266	0.003	2	0.045	2	5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-isopropyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide
267^	0.050	2	0.984	2	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
268^	0.003	2	0.021	2	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

269^	0.087	2	0.834	4	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
270^	0.007	2	0.033	4	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-6-ethyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
271^	0.011	2	0.180	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-isopropyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
272^	0.004	2	0.030	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-isopropyl-1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
273^	0.003	2	0.012	3	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
274^	0.695	2	4.773	3	*rel*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxamide
275^	0.007	2	0.030	5	*rel*-(4*R*,8*S*)-10-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-4,5,6,7,8,9-hexahydro-1*H*-4,8-epiminocycloocta[*c*]pyrazole-3-carboxamide
276^	0.002	2	0.028	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
277^	0.010	2	0.109	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
278	0.005	2	0.253	3	1-(3,3-dimethylbutan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
279	0.009	2	0.094	3	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isobutyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

280^	0.010	2	0.134	2	*rel-(R* or *S*)-6-(9-(4-(3,3-dimethylureido)benzyl)-4-methyl-10-oxo-3,4,7,8,9,10-hexahydropyrido[4',3':3,4]pyrazolo[1,5-*a*]pyrazin-2(1*H*)-yl)-*N,N*-dimethylnicotinamide
281^	0.017	2	0.212	2	*rel-(R* or *S*)-6-(9-(4-(3,3-dimethylureido)benzyl)-4-methyl-10-oxo-3,4,7,8,9,10-hexahydropyrido[4',3':3,4]pyrazolo[1,5-*a*]pyrazin-2(1*H*)-yl)-*N,N*-dimethylnicotinamide
282	0.001	2	0.009	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
283	0.002	5	0.011	4	(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
284	0.008	3	0.040	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
285^	0.001	2	0.007	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
286	0.663	2	> 3.065	4	5-(5-(2-(dimethylamino)-2-oxoethyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
287^	0.001	2	0.013	4	(*S*)-1-(cyclopropylmethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
288	1.639	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-8-oxa-2,5-diazaspiro[3.5]nonane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
289	0.312	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((3*aR*,6*aS*)-hexahydro-1*H*-furo[3,4-*c*]pyrrole-5-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
290	1.408	2	ND	ND	*rac*-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-((3*aR*,6*aS*)-2-oxohexahydro-2*H*-pyrrolo[3,4-*d*]oxazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

291	0.793	2	ND	ND	(*S*)-5-(5-(3-cyanopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
292	0.990	2	ND	ND	5-(5-(3-acetamidoazetidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
293	0.100	2	ND	ND	(*R*)-5-(5-(3,4-dimethyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
294	0.961	2	ND	ND	5-(5-(3,3-dimethyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
295	0.310	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-hydroxypiperidine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
296	0.523	2	ND	ND	5-(5-((3*aR*,6*aS*)-5-acetyloctahydropyrrolo[3,4-*c*]pyrrole-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
297	0.225	2	ND	ND	(*R*)-5-(5-(3-cyanopyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
298	2.545	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-2,5-diazaspiro[3.4]octane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
299	0.241	2	ND	ND	5-(5-((3*S*,5*R*)-4-acetyl-3,5-dimethylpiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
300	1.416	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-methyl-7-oxo-2,6-diazaspiro[3.4]octane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
301	0.001	4	0.008	4	(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

302	0.006	3	0.009	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
303^	0.022	2	0.334	3	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
304^	0.0003	2	0.004	5	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
305	0.005	2	0.007	3	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
306	0.007	2	0.033	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
307^	0.0005	2	0.007	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
308	0.287	2	0.718	2	1-(2-cyanoethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
309	1.713	2	4.098	2	1-(3-amino-3-oxopropyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
310^	0.008	2	0.115	3	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
311^	0.001	2	0.011	4	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
312^	0.010	2	0.163	3	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
313^	0.001	2	0.015	3	*rel-(R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-diethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

314	1.073	2	6.852	3	*rac*-(6*R*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-2-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
315	0.002	2	ND	ND	(*S*)-*N*-(4-(3,3-bis(methyl-d_3)ureido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
316^	3.769	1	ND	ND	*rel*-(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-2-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
317^	0.355	2	ND	ND	*rel*-(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-2-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
318^	0.0004	2	0.004	3	(*S*)-1-((*R**)-*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
319^	0.001	2	0.013	2	(*S*)-1-((*R**)-*sec*-butyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
320	0.005	2	0.135	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-(trifluoromethyl)cyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
321	0.003	2	0.022	3	*rac-(R)*-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(oxetan-3-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
322	0.077	2	1.351	3	*rac-(R)-N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
323	0.005	2	0.026	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((6-(3,3-dimethylureido)pyridin-3-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
324	0.005	2	0.018	3	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-((6-(3,3-dimethylureido)pyridin-3-yl)methyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
325	0.710	2	ND	ND	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

326	1.285	2	ND	ND	5-(5-(1-oxa-6-azaspiro[3.3]heptane-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
327	3.204	1	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(7-oxo-2,6-diazaspiro[3.4]octane-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
328	0.266	2	ND	ND	5-(5-(2,2-dimethyl-5-oxopiperazine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
329	1.050	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxo-1,8-diazaspiro[4.5]decane-8-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
330	1.980	2	ND	ND	5-(5-(3-acetamido-3-methylazetidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
331	0.606	2	ND	ND	*rac*-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((3*aR*,6*aR*)-hexahydro-2*H*-furo[2,3-*c*]pyrrole-5-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
332	0.160	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((2-hydroxyethyl)(methyl)carbamoyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
333	2.803	2	ND	ND	*rac*-5-(5-((3*R*,4*R*)-3,4-dimethoxypyrrolidine-1-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
334	0.176	2	ND	ND	*rac*-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-((3*aR*,6*aS*)-3-methyl-2-oxohexahydro-2*H*-pyrrolo[3,4-*d*]oxazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
335^	0.001	2	0.005	6	(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
336^	0.014	2	0.041	3	*rel*-(*R* or *S*)-7-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-5-ethyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
337	5.367	2	> 20.47	4	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-(methylamino)-2-oxoethyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

338	3.109	2	> 30.0	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(oxetan-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
339	6.546	2	> 23.12	4	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
340	0.276	2	2.343	3	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
341	0.004	2	0.028	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
342	0.003	2	0.015	3	(*S*)-*N*-(4-carbamoylbenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
343	0.001	2	0.009	4	(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
344	0.001	2	0.008	4	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-((*RS*)-1-methoxypropan-2-yl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
345	> 2.634	2	> 30.0	1	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
346	0.002	2	0.013	1	(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
347^	0.083	2	0.127	1	*rel*-(*R* or *S*)-1-(1-cyanopropan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
348^	0.043	2	0.036	1	*rel*-(*R* or *S*)-1-(1-cyanopropan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
349	0.002	2	0.011	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((6-(3,3-dimethylureido)pyridin-3-yl)methyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

350	0.002	2	0.006	4	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
351	0.073	2	0.129	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-hydroxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
352^	0.0003	2	0.003	5	(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
353^	0.004	2	0.047	3	(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
354^	0.004	2	0.024	3	(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
355^	0.0002	2	0.003	5	(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
356^	0.246	2	3.311	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
357^	0.001	2	0.020	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
358	0.051	2	0.112	2	*rac*-(*R*)-1-(1-cyanopropan-2-yl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
359^	0.358	2	0.869	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-hydroxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
360^	0.074	2	0.091	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(1-hydroxypropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
361^	0.158	2	> 4.082	4	*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

362^	0.838	2	> 3.489	4	*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydrofuran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
363	0.007	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-1,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
364	0.020	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
365	0.006	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydrothiazolo[5,4-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
366	0.029	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydropyrido[3,4-*b*]pyrazine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
367	0.072	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
368	0.005	3	ND	ND	5-(5-(2,4-dimethyl-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
369	0.038	3	ND	ND	5-(5-(1,3-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
370	0.011	3	ND	ND	5-(5-(2-cyclopropyl-6,7-dihydro-5*H*-pyrrolo[3,4-*d*]pyrimidine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
371	0.050	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
372	0.059	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

373	0.540	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
374	0.014	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydrothiazolo[5,4-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
375	0.015	4	1.962	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(8-methoxy-1,2,3,4-tetrahydro-2,7-naphthyridine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
376	0.010	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-1,6-naphthyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
377	0.021	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
378	0.015	2	ND	ND	5-(5-(2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
379	0.070	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydropyrido[4,3-*d*]pyrimidine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
380	0.538	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
381	0.033	3	ND	ND	5-(5-(2,3-dimethyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
382	0.137	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
383	0.049	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydroisoxazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

384	0.015	4	1.073	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methoxy-5,6,7,8-tetrahydro-1,6-naphthyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
385	0.004	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrazole-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
386	0.056	3	ND	ND	5-(5-(2-cyano-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
387	0.003	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methoxyisoindoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
388	0.008	2	0.029	2	(*S*)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
389	0.006	2	0.017	2	(*S*)-*N*-(4-carbamoylbenzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
390	0.039	2	0.104	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
391^	0.740	2	2.172	1	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
392^	0.568	2	1.082	1	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-methyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
393^	> 8.752	2	> 30.0	1	*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
394^	> 7.658	2	> 30.0	1	*rel*-(*R* or *S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(tetrahydro-2*H*-pyran-2-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

395	0.001	2	0.006	2	(*S*)-*N*-(4-carbamoylbenzyl)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
396	0.001	2	0.015	2	(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
397	0.001	2	0.009	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-ethyl-7-methyl-*N*-(4-(4-methyl-1*H*-imidazol-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
398	0.0003	2	0.007	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-ethyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
399	0.002	2	0.009	2	*rac*-(*R*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
400	1.042	2	2.574	2	5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-methyl-1',4',5',7'-tetrahydrospiro[cyclopropane-1,6'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide
401	0.032	3	ND	ND	5-(5-(1,3-dimethyl-1,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrazole-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
402	0.003	4	ND	ND	5-(5-(5,6-dihydro-4*H*-pyrrolo[3,4-*d*]thiazole-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
403	0.012	4	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydrothiazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
404	0.040	4	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
405	0.159	4	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-4,5,6,7-tetrahydro-3*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

406	0.011	4	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydrothiazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
407	0.010	3	0.100	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methoxy-5,6,7,8-tetrahydro-1,7-naphthyridine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
408	0.039	4	ND	ND	5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*d*]pyrimidine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
409	0.024	3	ND	ND	5-(5-(1,2-dimethyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
410	0.015	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-5,6,7,8-tetrahydro-1,6-naphthyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
411	0.008	3	ND	ND	5-(5-(5-cyanoisoindoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
412	0.396	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(7-hydroxy-1,2,3,4-tetrahydro-2,6-naphthyridine-2-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
413	0.082	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
414	0.066	3	ND	ND	5-(5-(2,3-dimethyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
415	0.003	2	ND	ND	5-(5-(4-cyanoisoindoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
416	0.029	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

417	0.017	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydro-1,7-naphthyridine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
418	0.061	2	ND	ND	5-(5-(1,3-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
419	0.044	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
420	0.017	4	0.125	3	5-(5-(1-cyclopropyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
421	0.018	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
422	0.019	3	ND	ND	5-(5-(7-cyano-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
423	0.029	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methyl-4,5,6,7-tetrahydrooxazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
424	0.046	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(7-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
425	0.034	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
426	0.013	2	ND	ND	(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methylisoindoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
427	0.282	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

428^	0.017	2	0.140	2	*rel*-(*R* or *S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
429^	0.001	2	0.006	2	*rel*-(*R* or *S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-ethyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
430	0.333	2	1.414	2	5-(5-(2-amino-2-oxoethyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
431	0.012	3	0.089	3	5-(5-(4-(dimethylcarbamoyl)isoindoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
432	0.186	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4,5,6,7-tetrahydroisoxazolo[4,5-*c*]pyridine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
433	0.276	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydropyrido[3,4-*d*]pyrimidine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
434	0.082	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1,2,3,4-tetrahydro-2,6-naphthyridine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
435	0.010	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1,2,3,4-tetrahydroisoquinoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
436	0.022	2	ND	ND	5-(5-(6-cyano-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
437	0.045	3	1.053	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-6-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
438	0.105	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

439	0.088	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-oxo-1,3,4,6-tetrahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
440	0.016	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(6-methyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
441	0.002	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(4-methylisoindoline-2-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
442	0.002	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(isoindoline-2-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
443	0.011	3	0.878	1	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-methoxy-5,6,7,8-tetrahydro-1,7-naphthyridine-7-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
444^	0.158	2	1.375	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,4-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
445^	0.002	2	0.021	2	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,4-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
446^	0.015	2	0.080	2	(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
447^	0.0004	2	> 0.413	2	(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
448^	0.013	2	> 30.0	1	(6*R*,7*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
449^	0.0002	2	0.004	3	(6*S*,7*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
450	0.021	3	0.093	3	(*S*)-*N*-(4-aminobenzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
451	0.003	2	0.047	2	(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

452	0.003	2	0.016	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
453	2.150	2	12.110	2	5-(5-carbamoylpyridin-2-yl)-1-isopropyl-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
454	0.128	2	0.720	2	1-isopropyl-5-(5-(methylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
455	0.311	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(3-methyl-4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-*a*]pyrazine-5-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
456	0.742	2	0.579	2	1-isopropyl-5-(5-(methylcarbamoyl)pyridin-2-yl)-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
457	5.961	1	5.010	2	5-(5-carbamoylpyridin-2-yl)-1-isopropyl-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
458	0.173	3	> 7.647	4	(*S*)-*N*-(3-carbamoyl-2-fluorophenyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
459	0.0003	2	0.002	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
460	0.0003	2	0.007	3	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
461^	0.0002	2	< 0.001	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
462^	0.0387	2	0.376	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
463	0.0027	2	0.023	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
464^	0.0002	2	0.002	4	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

465^	0.0518	2	0.682	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
466	0.002	2	0.018	2	(*S*)-5-(5-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
467^	0.3150	2	2.501	3	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
468^	0.0022	2	0.012	4	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(methylcarbamoyl)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
469	5.108	1	> 4.161	5	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
470	0.001	2	0.005	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
471	0.432	1	3.293	2	(*S*)-*N*-(4-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
472	0.041	1	0.120	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
473	0.0003	1	0.005	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
474^	0.040	1	0.085	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
475^	0.072	1	0.215	2	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-hydroxy-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
476	0.001	1	0.009	2	(*S*)-1-ethyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

477	0.0004	2	0.004	2	(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
478	0.002	2	0.017	2	(*S*)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
479	0.004	2	0.015	2	(*S*)-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
480	0.0003	2	0.003	2	(*S*)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
481	0.001	2	0.014	2	(*S*)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
482	0.007	2	0.025	3	(*S*)-1-ethyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
483	0.033	2	0.063	2	(*S*)-*N*-(4-carbamoylbenzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
484	0.026	2	0.108	2	(*S*)-1-ethyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
485	0.001	2	0.004	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-(piperidin-4-yloxy)piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
486	0.002	2	0.011	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
487	0.002	2	0.016	2	(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
488	0.003	2	0.027	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
489	0.018	2	0.017	2	(*S*)-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

490	0.013	2	0.050	2	(*S*)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-5-(5-(2-oxopyrrolidin-1-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
491	0.007	2	0.034	2	(*S*)-*N*-(4-aminobenzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
492	0.0005	2	0.004	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3-(4-(3,3-dimethylureido)benzyl)ureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
493^	0.028	2	0.203	2	*rel*-(*R* or *S*)-7-(difluoromethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
494^	0.0005	2	0.004	2	*rel*-(*R* or *S*)-7-(difluoromethyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
495	0.001	2	0.034	1	(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
496	0.004	2	0.016	2	(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
497	0.001	2	0.016	2	ethyl (*S*)-(4-((5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate
498	0.133	2	3.438	2	(*S*)-2-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)pyrimidine-5-carboxylic acid
499	0.0003	2	0.006	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-(4-(3,3-dimethylureido)benzyl)ureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
500	0.011	2	0.104	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

501	0.007	2	0.050	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-((4-(3,3-dimethylureido)benzyl)carbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
502	0.813	2	7.553	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
503	0.001	2	0.013	2	ethyl (*S*)-(4-((5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)carbamate
504	0.874	2	> 21.2	2	(*S*)-6-(3-((4-(3,3-dimethylureido)benzyl)carbamoyl)-1-isopropyl-7-methyl-1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)nicotinic acid
505	7.895	1	> 30.0	1	*rac*-(*R*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-2-oxopyrrolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
506^	0.002	2	0.014	3	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
507^	0.136	2	1.649	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
508^	0.007	2	0.020	3	(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
509^	3.316	1	8.170	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
510^	1.517	2	8.832	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
511^	0.006	2	0.029	2	(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
512^	0.240	2	2.508	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
513^	0.003	2	0.018	2	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-4-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

514	0.001	2	0.015	2	(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
515	0.001	2	0.006	2	(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
516	0.001	2	0.005	2	(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyridin-2-yl)-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
517	0.009	2	0.033	2	*(S)*-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
518	0.002	2	0.071	2	(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1*H*-imidazol-2-yl)benzyl)-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
519	0.008	2	0.219	1	(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1*H*-imidazol-2-yl)benzyl)-5-(5-(2-oxooxazolidin-3-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
520	0.001	2	0.022	1	(*S*)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-5-(5-(2-oxooxazolidin-3-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
521	0.002	2	0.034	2	(*S*)-5-(5-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
524	0.0001	1	0.006	3	(4*RS*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
525	0.002	4	0.007	6	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(piperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
526	4.009	1	2.037	2	5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-methylureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
527^	8.872	1	> 25.1	3	(S)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
528^	0.017	2	0.067	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-4-ethyl-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

529^	0.0001	1	0.004	2	(4*R*,7*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
530	0.0002	2	0.006	2	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
531	0.001	2	0.014	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-ethyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
532	0.001	2	0.004	2	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
533	0.005	2	0.018	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
534	0.033	2	0.155	2	(*S*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-6-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
535	0.005	2	0.013	3	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-((5-(3,3-dimethylureido)pyridin-2-yl)methyl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
536	0.004	2	0.031	2	(*S*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-6-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
537	0.001	2	0.010	2	*rac*-(*R*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
538^	0.0002	2	0.005	2	*rel*-(*R or S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
539^	0.013	2	0.072	2	*rel*-(*R or S*)-7-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-3-isopropyl-5-methyl-5,6,7,8-tetrahydroimidazo[1,5-*a*]pyrazine-1-carboxamide
540	0.027	2	0.076	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-6-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

546	0.0003	2	0.005	5	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
547^	0.0002	2	0.003	5	*rel*-(*R or S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
548^	0.015	2	0.199	3	*rel*-(*R or S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
549^	0.099	3	1.102	2	(*R*)-*N*-(4-(1*H*-imidazol-2-yl)benzyl)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
550^	0.011	3	0.085	3	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
551^	0.012	3	0.104	3	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(1-methylcyclopropyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
552^	0.034	3	0.087	3	(*R*)-5-(5-(dimethylcarbamoyl)pyrimidin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
553^	0.004	2	0.018	3	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-((*RS*)-1,1,1-trifluoropropan-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
555	0.005	2	0.052	2	5'-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1'-ethyl-1',4',5',6'-tetrahydrospiro[cyclopropane-1,7'-pyrazolo[4,3-*c*]pyridine]-3'-carboxamide
556^	0.058	3	0.196	3	(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-1-(tetrahydro-2*H*-pyran-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
557^	0.015	3	0.204	3	(*R*)-1-cyclobutyl-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
562	0.003	2	0.008	2	(*S*)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-*N*-(4-ureidobenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

563	0.202	3	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-5-(5-(4-(ethylsulfonyl)piperazine-1-carbonyl)pyridin-2-yl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
564	0.223	2	ND	ND	*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(1-methyl-2-oxo-1,8-diazaspiro[4.5]decane-8-carbonyl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
565	0.005	1	ND	ND	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(4-(((1-(2-methoxyethyl)piperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
566	0.002	2	0.015	3	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
567	0.001	2	0.013	3	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
568	0.002	2	0.013	3	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-((*R*)-3-(methylamino)piperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
569	0.004	2	0.020	3	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-((*S*)-3-(methylamino)piperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
570	0.003	2	0.027	2	(*S*)-*N*-(4-((*S*)-3-amino-3-methylpyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
571	0.004	2	0.020	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((S)-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
572	0.003	2	0.020	2	(*S*)-*N*-(4-((*R*)-3-amino-3-methylpyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
573	0.001	2	0.011	2	(*S*)-*N*-(4-((1*RS*,5*SR*)-3,8-diazabicyclo[3.2.1]octane-3-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

574	0.0005	3	0.011	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
575	0.001	3	0.010	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*S*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
576	0.004	2	0.019	2	(*S*)-*N*-(4-(1,4-diazepane-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
577	0.001	3	0.004	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-((*R*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
578	0.0005	2	0.005	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-((*S*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
579	0.0004	2	0.008	2	(*S*)-*N*-(4-(3-(2,2-difluoroethyl)ureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
580	0.001	2	0.011	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
581	0.003	2	0.024	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-methyl-3-(methylamino)azetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
583	0.001	2	0.017	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
584	0.001	2	0.012	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3-fluoroazetidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
585	0.006	2	0.037	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methylpiperidine-4-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

586	0.006	2	0.058	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(4-fluoro-1-methylpiperidine-4-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
587	0.014	2	0.122	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(1-methylpiperidine-4-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
588	0.075	2	0.875	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(5-fluoro-2-methoxy-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
589	0.003	2	0.019	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(2-fluoro-4-(piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
590	0.0004	2	0.010	2	(*S*)-*N*-(4-(3,3-difluoropyrrolidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
591	0.001	2	0.010	2	(*S*)-*N*-(4-(azetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
592	0.001	2	0.009	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(4-hydroxy-4-methylpiperidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
593	0.001	2	0.012	2	(*S*)-*N*-(4-(4-cyano-4-methylpiperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
594	0.002	2	0.025	2	(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(4-(2-oxopyridin-1(2*H*)-yl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
595	0.064	2	0.083	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
596	0.003	2	0.045	2	(*S*)-*N*-(3-chloro-4-(piperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

597	0.004	2	0.028	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(3-(methylamino)azetidine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
598	0.001	2	0.013	2	(*S*)-*N*-(4-(3-(2,2-difluoroethyl)-3-methylureido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
599	0.001	2	0.012	2	(*S*)-*N*-(4-(3,3-difluoroazetidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
601	0.312	2	2.102	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-((1-methylpiperidin-4-yl)carbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
602	0.001	2	0.014	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(1-methyl-1,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
603	0.003	2	0.031	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.4]octane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
604	0.004	2	0.029	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
605	0.004	2	0.037	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(methylcarbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
606	0.001	2	0.009	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
607	0.002	2	0.021	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

608	0.001	2	0.016	2	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
609	0.001	2	0.007	2	(*S*)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
610	0.002	2	0.017	2	(*S*)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
611	0.0002	2	0.005	2	(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
612	0.0005	2	0.010	2	(*S*)-5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
613	0.003	1	ND	ND	(*S*)-5-(5-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
614	0.0004	1	0.007	1	(*S*)-5-(4-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
615	0.002	1	0.013	1	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methyl-1,4-diazepane-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
616	0.001	1	0.006	1	(*S*)-*N*-(4-(4-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
617	0.178	1	0.502	1	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(((1-methylpiperidin-4-yl)methyl)carbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

618	0.127	1	0.612	1	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(((1-methylpiperidin-4-yl)methyl)carbamoyl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
619	0.003	1	0.019	1	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-(methylamino)azetidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
620	0.001	1	0.008	1	(*S*)-*N*-(4-([4,4'-bipiperidine]-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
621	0.007	1	0.031	1	(*S*)-*N*-(4-(1,6-diazaspiro[3.3]heptane-6-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
622	0.004	1	0.016	1	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2,9-diazaspiro[5.5]undecane-9-carboxamide
623	0.013	1	0.037	1	(*S*)-*N*-(4-(2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
624	0.001	1	0.018	1	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-(piperidin-4-ylmethyl)piperidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
625	0.010	1	0.024	1	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-3,9-diazaspiro[5.5]undecane-3-carboxamide
626	0.038	1	0.088	1	(*S*)-*N*-(4-(2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
627	0.007	1	0.023	1	(*S*)-*N*-(4-(3-aminoazetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
628	0.001	1	0.004	1	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-1-oxa-4,9-diazaspiro[5.5]undecane-9-carboxamide

629	0.121	1	0.390	1	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-methylazetidin-3-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
630	0.009	1	0.055	1	(*S*)-*N*-(2-chloro-4-(piperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
631	0.001	1	0.024	1	(*S*)-5-(5-(2*H*-1,2,3-triazol-2-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
632	0.005	1	0.039	1	(*S*)-*N*-(3-fluoro-4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
633	0.002	1	0.013	1	(*S*)-1-isopropyl-7-methyl-*N*-(4-(2-methyl-2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
634	0.004	1	0.029	1	(*S*)-1-isopropyl-7-methyl-*N*-(4-(7-methyl-2,7-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-5-(2-oxo-2*H*-[1,3'-bipyridin]-6'-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
635	0.014	1	0.071	1	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl((1-methylpiperidin-4-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
636	0.003	1	0.033	1	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(2-morpholinoethyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
637	0.013	1	0.048	1	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(piperidin-4-ylmethyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
638	0.001	1	0.004	1	(*S*)-*N*-(4-(4-amino-4-(methoxymethyl)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

639	0.001	1	0.008	1	(*S*)-*N*-(4-(4-amino-4-(methoxymethyl)piperidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
640	0.001	1	ND	ND	(*S*)-*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)octahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carboxamide
641	0.005	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
642	0.001	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-2-methyl-2,8-diazaspiro[4.5]decane-8-carboxamide
643	0.001	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-4-methyl-1-oxa-4,9-diazaspiro[5.5]undecane-9-carboxamide
644	0.001	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-2-methyl-2,9-diazaspiro[5.5]undecane-9-carboxamide
645	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(1-methyl-1,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
646	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(6-methyl-2,6-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
647	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(2-methyl-2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

648	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(4-methyl-4,7-diazaspiro[2.5]octane-7-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
649	0.001	1	0.024	1	(*S*)-5-(5-(1-cyclopropyl-1*H*-1,2,4-triazol-5-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
651	0.001	1	ND	ND	(*S*)-1-isopropyl-7-methyl-5-(2-methyl-1-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*c*]azepin-7-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
652	0.005	1	ND	ND	(*S*)-5-(4-(1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
653	0.003	1	ND	ND	(*S*)-5-(5-(1-cyclopropyl-1*H*-imidazol-2-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
654	0.002	2	ND	ND	(*S*)-5-(5-(1-(difluoromethyl)-1*H*-imidazol-2-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
655	0.002	2	ND	ND	(*S*)-5-(5-(4-cyclopropyl-4*H*-1,2,4-triazol-3-yl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
656	0.002	1	ND	ND	(*S*)-1-isopropyl-7-methyl-5-(4-(3-methyl-5-oxo-1,2,4-oxadiazol-4(5*H*)-yl)phenyl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
657	0.002	1	ND	ND	(*S*)-1-isopropyl-7-methyl-5-(4-methyl-5-oxo-2,3,4,5-tetrahydrobenzo[*f*][1,4]oxazepin-8-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
658	0.004	1	ND	ND	(*S*)-1-isopropyl-7-methyl-5-(5-(4-methyl-4*H*-1,2,4-triazol-3-yl)pyridin-2-yl)-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
659	0.008	1	ND	ND	(*S*)-*N*-(4-(3-(dimethylamino)-3-methylazetidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

660	0.004	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-9-methyl-3,9-diazaspiro[5.5]undecane-3-carboxamide
661	0.005	1	ND	ND	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(methyl(((1*R*,5*S*,6*r*)-3-methyl-3-azabicyclo[3.1.0]hexan-6-yl)methyl)carbamoyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
662	0.003	1	ND	ND	(*S*)-5-(4-(((1-benzylpiperidin-4-yl)methyl)(methyl)carbamoyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
669	0.201	1	ND	ND	(*S*)-3-(4-((4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)carbamoyl)piperazin-1-yl)propanoic acid
670^	0.001	1	ND	ND	(*S*)-*N*-(4-((*R**)-3-amino-3-(2-methoxyethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
671^	0.003	1	ND	ND	(*S*)-*N*-(4-((*R**)-3-amino-3-(2-methoxyethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
672^	0.001	1	ND	ND	(*S*)-*N*-(4-((*R**)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
673^	0.002	1	ND	ND	(*S*)-*N*-(4-((*R**)-3-amino-3-(methoxymethyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
674	0.0002	1	ND	ND	(*S*)-5-(4-(1*H*-1,2,3-triazol-1-yl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

675	0.034	1	ND	ND	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carbonyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
676	0.0003	1	ND	ND	(*S*)-5-(4-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)phenyl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
678	0.003	1	ND	ND	(*S*)-*N*-(4-((*R*)-3-(dimethylamino)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
679	0.003	1	ND	ND	(7*S*)-*N*-(4-(3-(dimethylamino)-3-methylpyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
680	0.002	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*S*)-3,4-dimethylpiperazine-1-carboxamido)-3-fluorobenzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
681	0.003	1	ND	ND	(*S*)-*N*-(4-((*S*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
682	0.004	1	ND	ND	(*S*)-*N*-(4-((*R*)-3-(dimethylamino)piperidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
683	0.003	1	ND	ND	(*S*)-*N*-(4-((*S*)-3-(dimethylamino)piperidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
684	0.002	1	ND	ND	(*S*)-*N*-(4-((*R*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)-3-fluorobenzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
685	0.002	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(3-(3-methylazetidin-3-yl)ureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

686	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*R*)-3,4-dimethylpiperazine-1-carboxamido)-3-fluorobenzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
687	0.001	1	ND	ND	(*R*)-*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)octahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carboxamide
688	0.001	1	ND	ND	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-((*R*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
689	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-((*R*)-3-(methoxymethyl)piperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
690	0.001	1	ND	ND	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(3-fluoro-4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
691	0.001	1	ND	ND	(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-7-methyl-*N*-(4-((*R*)-octahydropyrrolo[1,2-*a*]pyrazine-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
692	0.0003	1	ND	ND	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
693	0.016	1	ND	ND	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
694	0.0003	1	ND	ND	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
695	0.032	1	ND	ND	*rel*-(*R* or *S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-ethyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

699	0.004	1	0.027	1	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-((6-(piperazine-1-carboxamido)pyridin-3-yl)methyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
700	0.005	1	0.022	1	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-((5-(piperazine-1-carboxamido)pyridin-2-yl)methyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
701	0.0004	1	ND	ND	*rac*-(*R*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
702	0.010	1	ND	ND	*rel*-(*R* or *S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
703	0.001	1	ND	ND	*rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
704	0.001	1	ND	ND	*rac*-(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(piperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
705	0.0002	1	ND	ND	*rel*-(*R* or *S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-*N*-(4-(4-methylpiperazine-1-carboxamido)benzyl)-7-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
706	0.027	1	0.191	1	(*S*)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-5-(4-(4-methylpiperazine-1-carbonyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
708	0.001	1	0.008	1	(*S*)-*N*-(4-(4-amino-4-(2-methoxyethyl)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
711	0.0005	1	0.018	1	(*S*)-5-(4-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)phenyl)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

712	0.003	1	0.064	1	(*S*)-*N*-(2-chloro-4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
713	0.003	1	0.022	1	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R**)-3-methyl-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
714	0.004	1	0.028	1	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R**)-3-methyl-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
715	0.005	2	0.068	2	(*S*)-*N*-(3-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-5-(4-(2-oxopyridin-1(2*H*)-yl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
716	0.003	2	0.025	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-ethyl-*N*-(3-fluoro-4-(3-(methylamino)azetidine-1-carboxamido)benzyl)-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
717	0.003	2	0.029	2	(*S*)-*N*-(3-chloro-4-(4-methylpiperazine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
718	0.001	2	0.018	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(2-fluoro-4-(4-methylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
719	1.002	2	3.690	2	(*S*)-*N*-(4-carbamoylbenzyl)-1-isopropyl-7-methyl-5-(5-(1-methyl-1*H*-imidazol-2-yl)pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
721	0.012	2	0.102	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(3-fluoro-4-(1-methylpiperidine-4-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
722	0.008	2	0.040	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-((*R*)-3-(methylamino)pyrrolidine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
723	0.128	2	0.665	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methyloxazol-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

724	0.129	2	5.061	2	(*R*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methylpyrazin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
725	0.177	2	4.458	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methyl-1*H*-pyrazol-3-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
726	0.123	3	5.676	3	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methylpyridin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
727	0.011	2	0.383	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methylpyridazin-3-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
728	0.231	2	4.213	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(2-methylpyrimidin-4-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
729	0.683	2	4.327	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylthiazol-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
730	>10	1	>15.12	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(4-methylpyrimidin-2-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
731	0.082	2	1.246	2	(*S*)-*N*-(4-(5-amino-4-methoxypyrimidin-2-yl)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
732	0.088	2	3.073	2	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methyl-1*H*-pyrazol-4-yl)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
733	0.342	1	ND	ND	(*S*)-3-(3-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)-1-methylureido)propanoic acid
734	0.038	1	ND	ND	(*S*)-1-((4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)-2-fluorophenyl)carbamoyl)piperidine-4-carboxylic acid
735	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*S*)-3,4-dimethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

736	0.001	1	ND	ND	(*S*)-*N*-(4-((*S*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
737	0.001	1	ND	ND	(*S*)-*N*-(4-(((*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)octahydro-2*H*-pyrido[1,2-*a*]pyrazine-2-carboxamide
738	0.001	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-4-methyl-1-oxa-4,9-diazaspiro[5.5]undecane-9-carboxamide
739	0.002	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(3-(3-methylazetidin-3-yl)ureido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
740	0.002	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(1-methyl-1,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
741	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methyl-2,6-diazaspiro[3.5]nonane-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
742	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(2-methyl-2,7-diazaspiro[3.5]nonane-7-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
743	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-((*R*)-3,4-dimethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
745	0.001	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-*N*-(4-(4-ethylpiperazine-1-carboxamido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
746	0.001	1	ND	ND	(*S*)-*N*-(4-(3-(dimethylamino)azetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
747	0.001	1	ND	ND	(*S*)-*N*-(4-((*S*)-3-(dimethylamino)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide

748	0.001	1	ND	ND	(*S*)-*N*-(4-(3-(dimethylamino)-3-methylazetidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
749	0.0004	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-9-methyl-3,9-diazaspiro[5.5]undecane-3-carboxamide
750	0.001	1	ND	ND	(*S*)-*N*-(4-((*R*)-3-(dimethylamino)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
751	0.009	1	ND	ND	(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-*N*-(4-(6-methyl-2,6-diazaspiro[3.3]heptane-2-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
752	0.002	1	ND	ND	(7*S*)-*N*-(4-(3-(dimethylamino)-3-methylpyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
753	0.0005	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-methyl-2,8-diazaspiro[4.5]decane-8-carboxamide
754	0.002	1	ND	ND	(*S*)-*N*-(4-((*R*)-3-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
755	0.002	1	ND	ND	(*S*)-*N*-(4-((*S*)-3-(dimethylamino)piperidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
756	0.001	1	ND	ND	(*S*)-*N*-(4-((*R*)-3-((dimethylamino)methyl)pyrrolidine-1-carboxamido)benzyl)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide
757	0.0003	1	ND	ND	(*S*)-*N*-(4-((5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamido)methyl)phenyl)-2-methyl-2,9-diazaspiro[5.5]undecane-9-carboxamide

Prophetic Deuterated Analogs

General methods / reviews of obtaining metabolite profile and identifying metabolites of a compound are described in: Dalvie, et al., "Assessment of Three Human in Vitro Systems in

the Generation of Major Human Excretory and Circulating Metabolites," Chemical Research in Toxicology, 2009, 22, 2, 357-368, tx8004357 (acs.org); King, R., "Biotransformations in Drug Metabolism," Ch.3, Drug Metabolism Handbook Introduction, https://doi.org/10.1002/9781119851042.ch3; Wu, Y., et al, "Metabolite Identification in the Preclinical and Clinical Phase of Drug Development," Current Drug Metabolism, 2021, 22, 11, 838-857, 10.2174/1389200222666211006104502; Godzien, J., et al, "Chapter Fifteen - Metabolite Annotation and Identification".

Numerous publicly available and commercially available software tools are available to aid in the predictions of metabolic pathways and metabolites of compounds. Examples of such tools include, BioTransofrmer 3.0 (biotransformer.ca/new), which predicts the metabolic biotransformations of small molecules using a database of known metabolic reactions; MetaSite (moldiscovery.com/software/metasite/), which predicts metabolic transformations related to cytochrome P450 and flavin-containing monooxygenase mediated reactions in phase I metabolism; and Lhasa Meteor Nexus (lhasalimited.org/products/meteor-nexus.htm) offers prediction of metabolic pathways and metabolite structures using a range of machine learning models, which covers phase I and phase II biotransformations of small molecules.

Predicted deuterated analogs in the examples may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased in vivo half-life, reduced dosage requirements, increased STAT6 inhibition (competitive or time dependent), or an improvement in therapeutic index or tolerability.

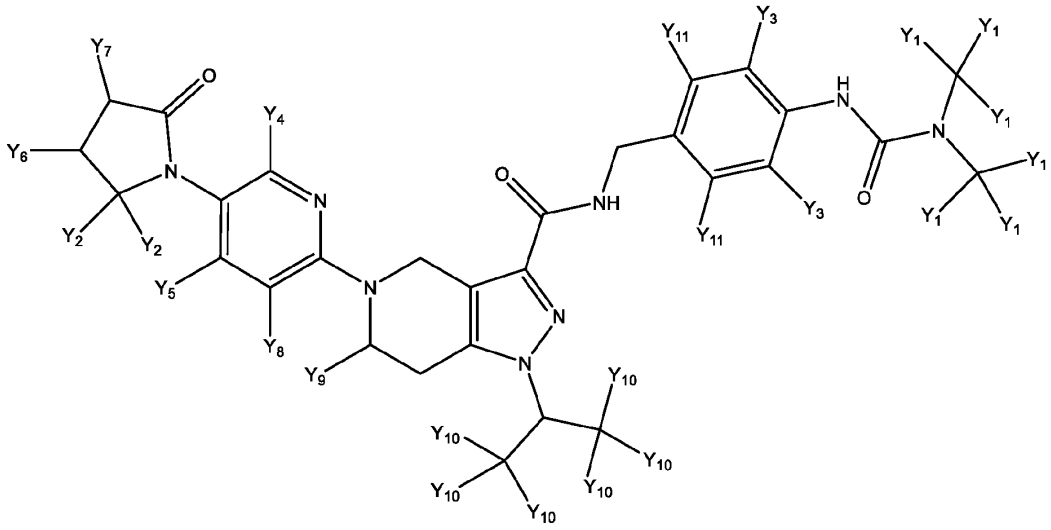
A person with ordinary skill may make additional deuterated analogs of the disclosed compounds with different combinations of deuterium replacing hydrogen. Such additional deuterated analogs may provide similar therapeutic advantages that may be achieved by the deuterated analogs as illustrated below.

In the examples, the "Y_i" is used to indicate the order of the sites most likely to be metabolized based on MetaSite predictions for the respective compound, where i=1 indicates the most likely, i=2 indicates the second most likely site and so on. It is noted that where Y_i is indicated as being deuterated, D, each Y_i independently can be D as long as at least one Y_i is D. For example, if Y_1 is deuterated and there are two Y_1 groups in the compound, then one or both groups can be deuterated as long as at least one Y_1 group is deuterated.

These examples are not intended to be limited to the specific compounds or locations of deuteration.

Example D1

Formula D1 is the generic formula of deuterated Example 1, wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, and Y_{10} are each independently H or D. Table 4 shows some examples of deuterated compounds based on the most likely metabolized sites that can be applied to the compounds predicted by MetaSite.



D1

Table 4

Deuteration Example	Y_1	Y_2	Y_3 and/ or Y_{11}	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}
D1A	D	H	H	H	H	H	H	H	H	H
D1B	D	D	H	H	H	H	H	H	H	H
D1C	D	D	D	H	H	H	H	H	H	H
D1D	D	H	D	H	H	H	H	H	H	H
D1E	D	H	H	D	H	H	H	H	H	H
D1F	D	H	H	H	D	H	H	H	H	H
D1G	D	H	H	H	H	D	H	H	H	H
D1H	D	H	H	H	H	H	D	H	H	H
D1I	D	H	H	H	H	H	H	D	H	H
D1J	D	H	H	H	H	H	H	H	D	H
D1K	D	H	H	H	H	H	H	H	H	D
D1L	D	D	D	D	H	H	H	H	H	H
D1M	H	D	D	H	H	H	H	H	H	H
D1N	H	D	H	D	H	H	H	H	H	H
D1O	H	D	H	H	D	H	H	H	H	H
D1P	H	D	H	H	H	D	H	H	H	H
D1Q	H	D	H	H	H	H	D	H	H	H
D1R	H	D	H	H	H	H	H	D	H	H
D1S	H	D	H	H	H	H	H	H	D	H
D1T	H	D	H	H	H	H	H	H	H	D
D1U	D	H	D	D	H	H	H	H	H	H
D1V	D	D	H	D	H	H	H	H	H	H

Example D2

Formula D2 is the generic formula of deuterated Example 2, wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, and Y_{10} are each independently H or D. Table 5 shows some examples of deuterated compounds based on the most likely metabolized sites that can be applied to the compounds predicted by MetaSite.

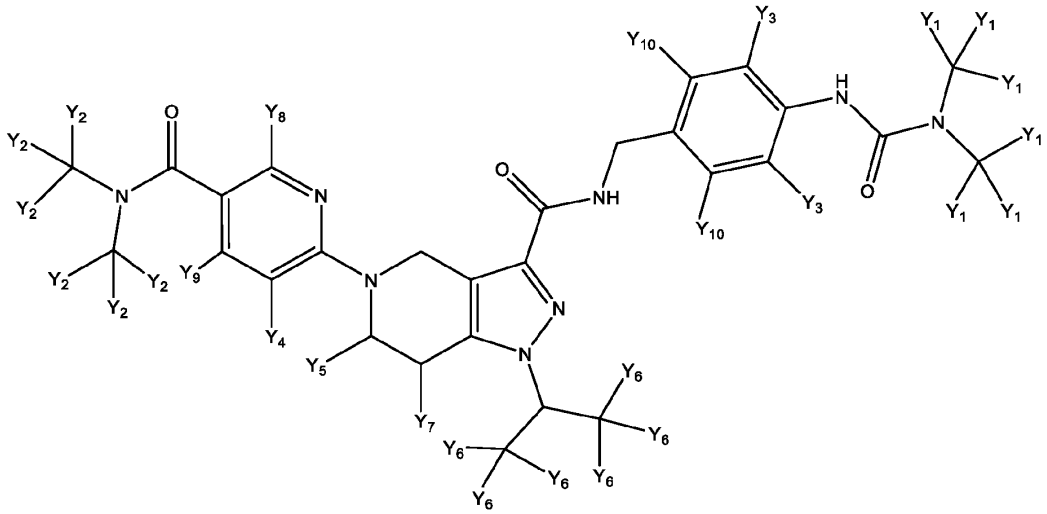


Table 5										
Deuteration Example	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}
D2A	D	H	H	H	H	H	H	H	H	H
D2B	D	D	H	H	H	H	H	H	H	H
D2C	D	D	D	H	H	H	H	H	H	H
D2D	D	H	D	H	H	H	H	H	H	H
D2E	D	H	H	D	H	H	H	H	H	H
D2F	D	H	H	H	D	H	H	H	H	H
D2G	D	H	H	H	H	D	H	H	H	H
D2H	D	H	H	H	H	H	D	H	H	H
D2I	D	H	H	H	H	H	H	D	H	H
D2J	D	H	H	H	H	H	H	H	D	H
D2K	D	H	H	H	H	H	H	H	H	D
D2L	D	D	D	D	H	H	H	H	H	H
D2M	H	D	D	H	H	H	H	H	H	H
D2N	H	D	H	D	H	H	H	H	H	H
D2O	H	D	H	H	D	H	H	H	H	H
D2P	H	D	H	H	H	D	H	H	H	H
D2Q	H	D	H	H	H	H	D	H	H	H
D2R	H	D	H	H	H	H	H	D	H	H
D2S	H	D	H	H	H	H	H	H	D	H
D2T	H	D	H	H	H	H	H	H	H	D
D2U	D	H	D	D	H	H	H	H	H	H
D2V	D	D	H	D	H	H	H	H	H	H

Example D6

Formula D6 is the generic formula of deuterated Example 6, wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, and Y_{10} are each independently H or D. Table 6 shows some examples of deuterated compounds based on the most likely metabolized sites that can be applied to the compounds predicted by MetaSite.

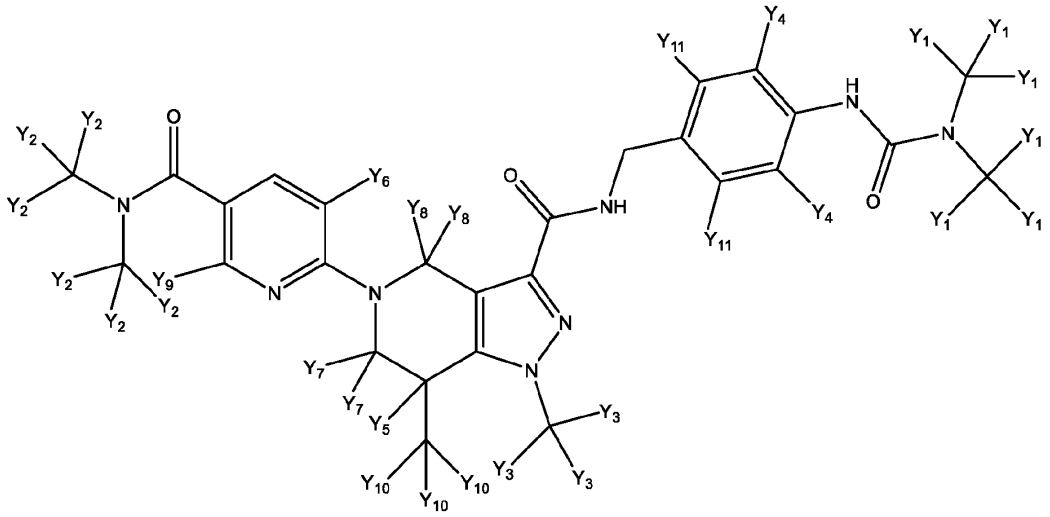


Table 6										
Deuteration Example	Y_1	Y_2	Y_3 and/ or Y_{11}	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}
D6A	D	H	H	H	H	H	H	H	H	H
D6B	D	D	H	H	H	H	H	H	H	H
D6C	D	D	D	H	H	H	H	H	H	H
D6D	D	H	D	H	H	H	H	H	H	H
D6E	D	H	H	D	H	H	H	H	H	H
D6F	D	H	H	H	D	H	H	H	H	H
D6G	D	H	H	H	H	D	H	H	H	H
D6H	D	H	H	H	H	H	D	H	H	H
D6I	D	H	H	H	H	H	H	D	H	H
D6J	D	H	H	H	H	H	H	H	D	H
D6K	D	H	H	H	H	H	H	H	H	D
D6L	D	D	D	D	H	H	H	H	H	H
D6M	H	D	D	H	H	H	H	H	H	H
D6N	H	D	H	D	H	H	H	H	H	H
D6O	H	D	H	H	D	H	H	H	H	H
D6P	H	D	H	H	H	D	H	H	H	H
D6Q	H	D	H	H	H	H	D	H	H	H
D6R	H	D	H	H	H	H	H	D	H	H
D6S	H	D	H	H	H	H	H	H	D	H
D6T	H	D	H	H	H	H	H	H	H	D
D6U	D	H	D	D	H	H	H	H	H	H
D6V	D	D	H	D	H	H	H	H	H	H

Example D31

Formula D31 is the generic formula of deuterated Example 31, wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, and Y_{10} are each independently H or D. Table 7 shows some examples of deuterated compounds based on the most likely metabolized sites that can be applied to the compounds predicted by MetaSite.

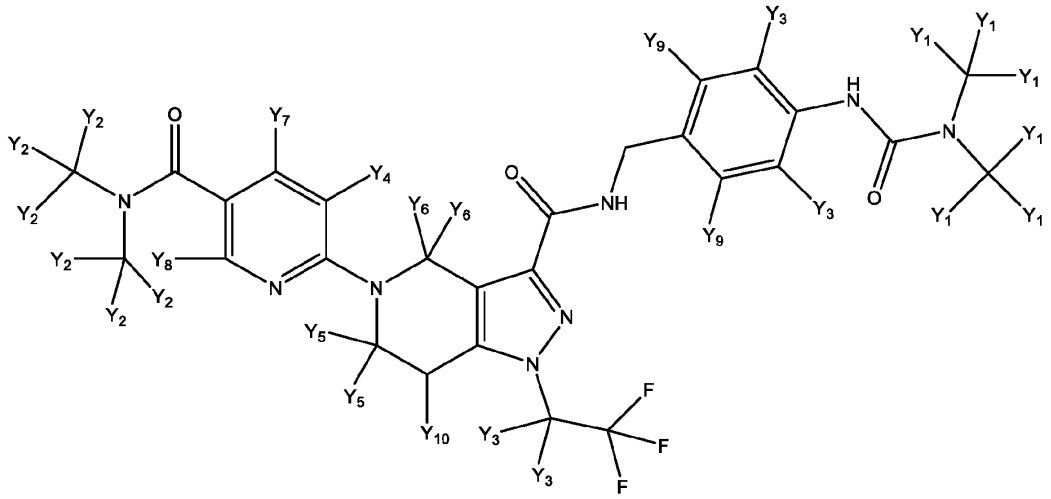


Table 7										
Deuteration Example	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}
D31A	D	H	H	H	H	H	H	H	H	H
D31B	D	D	H	H	H	H	H	H	H	H
D31C	D	D	D	H	H	H	H	H	H	H
D31D	D	H	D	H	H	H	H	H	H	H
D31E	D	H	H	D	H	H	H	H	H	H
D31F	D	H	H	H	D	H	H	H	H	H
D31G	D	H	H	H	H	D	H	H	H	H
D31H	D	H	H	H	H	H	D	H	H	H
D31I	D	H	H	H	H	H	H	D	H	H
D31J	D	H	H	H	H	H	H	H	D	H
D31K	D	H	H	H	H	H	H	H	H	D
D31L	D	D	D	D	H	H	H	H	H	H
D31M	H	D	D	H	H	H	H	H	H	H
D31N	H	D	H	D	H	H	H	H	H	H
D31O	H	D	H	H	D	H	H	H	H	H
D31P	H	D	H	H	H	D	H	H	H	H
D31Q	H	D	H	H	H	H	D	H	H	H
D31R	H	D	H	H	H	H	H	D	H	H
D31S	H	D	H	H	H	H	H	H	D	H
D31T	H	D	H	H	H	H	H	H	H	D
D31U	D	H	D	D	H	H	H	H	H	H
D31V	D	D	H	D	H	H	H	H	H	H

Example D33

Formula D33 is the generic formula of deuterated Example 33, wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, and Y_{10} are each independently H or D. Table 8 shows some examples of deuterated compounds based on the most likely metabolized sites that can be applied to the compounds predicted by MetaSite.

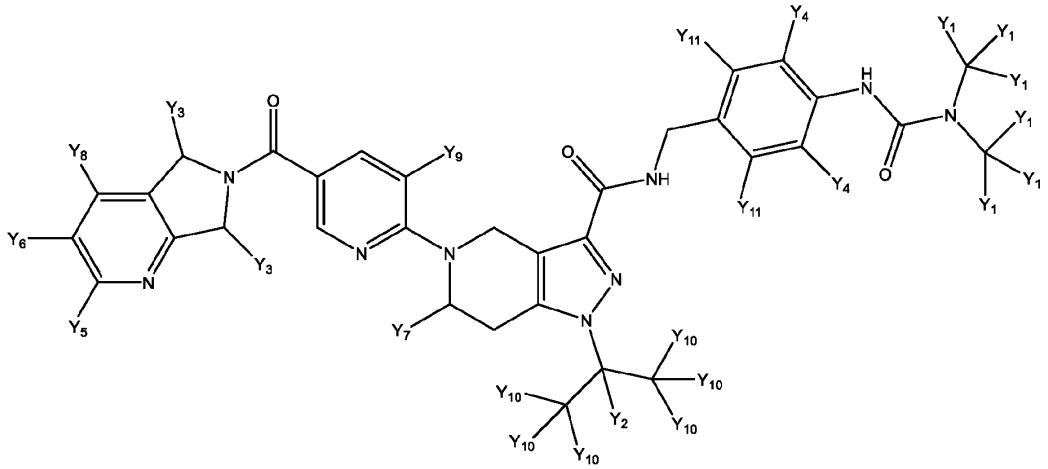


Table 8										
Deuteration Example	Y_1	Y_2	Y_3	Y_4 and/ or Y_{11}	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}
D33A	D	H	H	H	H	H	H	H	H	H
D33B	D	D	H	H	H	H	H	H	H	H
D33C	D	D	D	H	H	H	H	H	H	H
D33D	D	H	D	H	H	H	H	H	H	H
D33E	D	H	H	D	H	H	H	H	H	H
D33F	D	H	H	H	D	H	H	H	H	H
D33G	D	H	H	H	H	D	H	H	H	H
D33H	D	H	H	H	H	H	D	H	H	H
D33I	D	H	H	H	H	H	H	D	H	H
D33J	D	H	H	H	H	H	H	H	D	H
D33K	D	H	H	H	H	H	H	H	H	D
D33L	D	D	D	D	H	H	H	H	H	H
D33M	H	D	D	H	H	H	H	H	H	H
D33N	H	D	H	D	H	H	H	H	H	H
D33O	H	D	H	H	D	H	H	H	H	H
D33P	H	D	H	H	H	D	H	H	H	H
D33Q	H	D	H	H	H	H	D	H	H	H
D33R	H	D	H	H	H	H	H	D	H	H
D33S	H	D	H	H	H	H	H	H	D	H
D33T	H	D	H	H	H	H	H	H	H	D
D33U	D	H	D	D	H	H	H	H	H	H
D33V	D	D	H	D	H	H	H	H	H	H

Example D128

Formula D128 is the generic formula of deuterated Example 128, wherein Y1, Y2, Y3, Y4, Y5, Y6, Y7, Y8, Y9, and Y10 are each independently H or D. Table 9 shows some examples of deuterated compounds based on the most likely metabolized sites that can be applied to the compounds predicted by MetaSite.

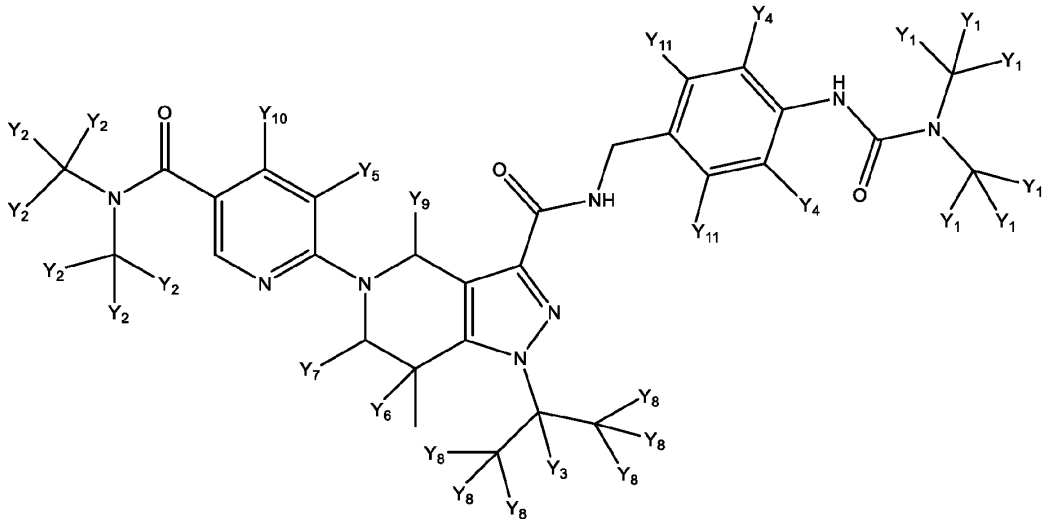


Table 9										
Deuteration Example	Y_1	Y_2	Y_3	Y_4 and/ or Y_{11}	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}
D128A	D	H	H	H	H	H	H	H	H	H
D128B	D	D	H	H	H	H	H	H	H	H
D128C	D	D	D	H	H	H	H	H	H	H
D128D	D	H	D	H	H	H	H	H	H	H
D128E	D	H	H	D	H	H	H	H	H	H
D128F	D	H	H	H	D	H	H	H	H	H
D128G	D	H	H	H	H	D	H	H	H	H
D128H	D	H	H	H	H	H	D	H	H	H
D128I	D	H	H	H	H	H	H	D	H	H
D128J	D	H	H	H	H	H	H	H	D	H
D128K	D	H	H	H	H	H	H	H	H	D
D128L	D	D	D	D	H	H	H	H	H	H
D128M	H	D	D	H	H	H	H	H	H	H
D128N	H	D	H	D	H	H	H	H	H	H
D128O	H	D	H	H	D	H	H	H	H	H
D128P	H	D	H	H	H	D	H	H	H	H
D128Q	H	D	H	H	H	H	D	H	H	H
D128R	H	D	H	H	H	H	H	D	H	H
D128S	H	D	H	H	H	H	H	H	D	H
D128T	H	D	H	H	H	H	H	H	H	D
D128U	D	H	D	D	H	H	H	H	H	H
D128V	D	D	H	D	H	H	H	H	H	H

Example D132

Formula D132 is the generic formula of deuterated Example 132, wherein Y1, Y2, Y3, Y4, Y5, Y6, Y7, Y8, Y9, and Y10 are each independently H or D. Table 10 shows some examples of deuterated compounds based on the most likely metabolized sites that can be applied to the compounds predicted by MetaSite.

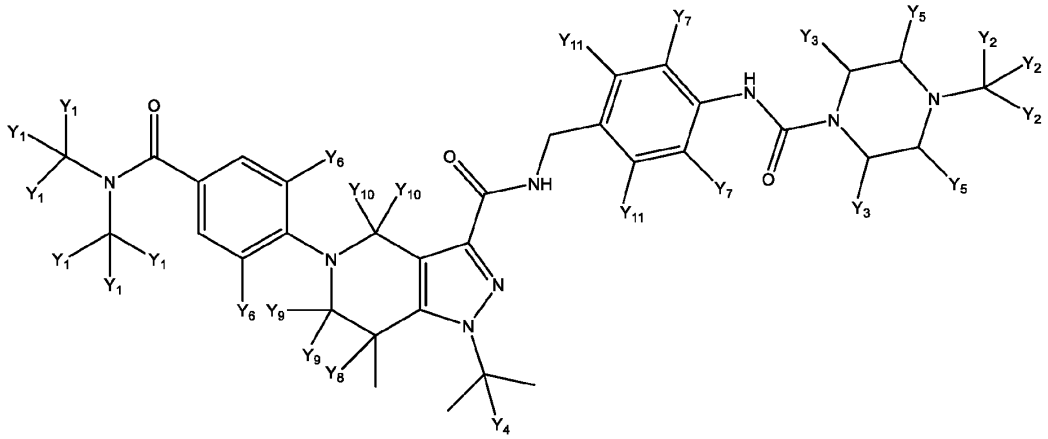


Table 10										
Deuteration Example	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7 and/ or Y_{11}	Y_8	Y_9	Y_{10}
D132A	D	H	H	H	H	H	H	H	H	H
D132B	D	D	H	H	H	H	H	H	H	H
D132C	D	D	D	H	H	H	H	H	H	H
D132D	D	H	D	H	H	H	H	H	H	H
D132E	D	H	H	D	H	H	H	H	H	H
D132F	D	H	H	H	D	H	H	H	H	H
D132G	D	H	H	H	H	D	H	H	H	H
D132H	D	H	H	H	H	H	D	H	H	H
D132I	D	H	H	H	H	H	H	D	H	H
D132J	D	H	H	H	H	H	H	H	D	H
D132K	D	H	H	H	H	H	H	H	H	D
D132L	D	D	D	D	H	H	H	H	H	H
D132M	H	D	D	H	H	H	H	H	H	H
D132N	H	D	H	D	H	H	H	H	H	H
D132O	H	D	H	H	D	H	H	H	H	H
D132P	H	D	H	H	H	D	H	H	H	H
D132Q	H	D	H	H	H	H	D	H	H	H
D132R	H	D	H	H	H	H	H	D	H	H
D132S	H	D	H	H	H	H	H	H	D	H
D132T	H	D	H	H	H	H	H	H	H	D
D132U	D	H	D	D	H	H	H	H	H	H
D132V	D	D	H	D	H	H	H	H	H	H

It will be apparent to those skilled in the art that various modifications and variations may be made in the present disclosure without departing from the scope or spirit of the disclosure. Other aspects of the disclosure will be apparent to those skilled in the art from consideration of the specification and practice of the disclosure disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the disclosure being indicated by the following claims.

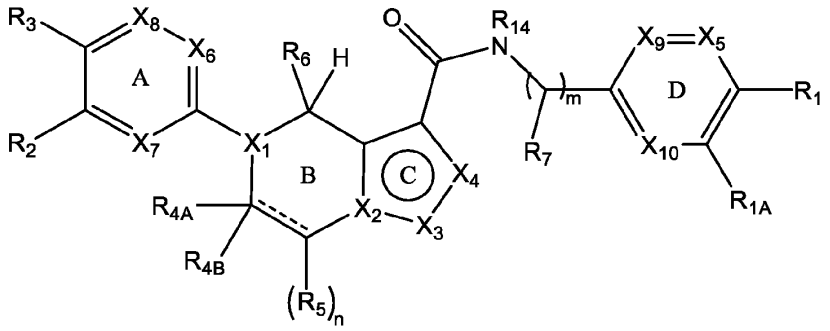
All references cited herein, including patents, patent applications, papers, textbooks, and the like, and the references cited therein, to the extent that they are not already, are hereby incorporated by reference in their entireties. In the event that one or more of the incorporated

literature and similar materials differs from or contradicts this application, including but not limited to defined terms, term usage, described techniques, or the like, this application controls.

CLAIMS

We claim:

1. A compound of Formula I, or a pharmaceutically acceptable salt thereof:



I

wherein

X_1 is CH, CNH_2, or N;

X_2 is C or N;

X_3 is CR_{13}, N, NR_{13}, O, or S;

X_4 is CH, N, or NR_{13};

X_5 is CR_{1B} or N;

X_6 is CH or N;

X_7 is CH, N, or CF;

X_8 is CH or N;

X_9 is CR_{1B} or N;

X_{10} is CR_{1B} or N;

R_1 is $-NHR_8$, -OH, $-C_{2-5}$ heterocycle, or $-C_{1-3}$ alkyl; wherein the $-C_{2-5}$ heterocycle of R_1 is optionally substituted with one, two, or three of $-C_{1-3}$ alkyl, $-C_{1-3}$ oxoalkyl, $-C_{3-5}$ heterocycloalkyl, $-C_{3-5}$ hydroxyheterocycloalkyl, $-C_{3-5}$ aminoheterocycloalkyl, or oxo; wherein the $-C_{1-3}$ alkyl of R_1 is optionally substituted with one, two, or three of oxo, $-NR_{10A}R_{11}$, or $-NR_{10}R_{11}$;

R_{1A} is H, halogen, or $-CH_3$; or

R_1 and R_{1A} form a C_{5-7} heterocycloalkyl fused to Ring D or a C_{5-7} heteroaryl fused to Ring D; wherein the C_{5-7} heterocycloalkyl or the C_{5-7} heteroaryl is optionally substituted with oxo;

each R_{1B} independently is H, $-CH_3$, F, Cl, or methoxy;

R_2 is H, $-C_{1-3}$ alkyl, $-C_{1-3}$ alkoxy, $-C_{1-3}$ fluoroalkyl, or halogen;

R_3 is $-C_{1-3}$ alkyl, $-C_{2-10}$ heterocycle, $-P(=O)(CH_3)_2$, $-S(=O)CH_3$, $-NH-S(=O)_2CH_3$, or $-NH-C(=O)-C_{1-3}$ alkyl; wherein the $-C_{1-3}$ alkyl of R_3 is optionally substituted with one, two, or three of oxo, halogen, $-C_{3-6}$ cycloalkyl, -OH, $-NR_{12}R_{12A}$, or cyano; wherein the $-C_{2-10}$ heterocycle is

optionally substituted with one, two, or three of -OH, halogen, -C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy, -C_{1-3} alkyl, -C_{1-3} fluoroalkyl, cyclopropyl, or oxo; or

R_2 and R_3 form a C_{3-6} heterocycle fused to Ring A optionally substituted with one, two, or three of -C_{1-3} alkyl, -C_{2-3} oxoalkyl, or oxo;

R_{4A} is H, -OH, -C_{1-3} fluoroalkyl, or -C_{1-3} alkyl;

R_{4B} is H or is absent; or

R_{4A} and R_{4B} form cyclopropyl;

each R_5 independently is H, halogen, -OH, cyclopropyl, -C_{1-3} fluoroalkyl, or -C_{1-3} alkyl; or two R_5 groups form cyclopropyl;

R_6 is H, -OH, or -C_{1-3} alkyl; or

R_{4A} and R_6 or one R_5 and R_6 form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge; or

R_{4B} and one R_5 form a C_{3-5} cycloalkyl fused to Ring B;

R_7 is H, -C_{1-3} alkyl, or -C_{1-3} hydroxyalkyl;

R_8 is H, -C_{1-3} alkyl, -SO_2CH_3, or a -C_{3-4} heterocycle; wherein the -C_{1-3} alkyl of R_8 is optionally substituted with one, two, or three of oxo, -C_{3-9} heterocycloalkyl, -C_{1-3} alkoxy, cyanoimine, or -NR_9R_{10}; wherein the -C_{3-4} heterocycle of R_8 is optionally substituted with one, two, or three of oxo, halogen, -C_{0-1} alkylene-$NR_{10}R_{11}$, -OH, -C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy optionally substituted with -$NR_{10}R_{11}$, -C_{1-3} alkyl-C_{1-3} alkoxy, -C_{1-3} oxoalkyl, or -C_{1-3} alkyl; wherein the -C_{3-9} heterocycloalkyl of R_8 is optionally substituted with one, two, or three of -C_{1-3} alkyl, -OH, -C_{1-3} hydroxyalkyl, -O-C_{1-3} hydroxyalkyl, -C_{1-3} alkoxy, -C_{1-3} alkyl-C_{1-3} alkoxy, halogen, -C_{1-3} fluoroalkyl, -C_{1-3} fluoroalkoxy, cyano, -C_{1-3} cyanoalkyl, -C_{0-1} alkylene-C_{3-5} heterocycloalkyl, -O-C_{3-5} heterocycloalkyl, or -C_{0-1} alkylene-$NR_{10}R_{11}$;

R_9 is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_9 is optionally substituted with one, two, or three of -C_{3-5} cycloalkyl, -C_{3-5} heterocycloalkyl, or methoxy; wherein the -C_{3-5} cycloalkyl of R_9 is optionally substituted with one or two of -OH or -C_{1-3} alkyl;

each R_{10} independently is H or -C_{1-4} alkyl;

R_{10A} is -C_{0-1} alkylene-C_{3-5} heterocycloalkyl optionally substituted with -C_{1-3} alkyl;

each R_{11} independently is H or -C_{1-3} alkyl;

R_{12} is H, -C_{1-3} alkyl, -C_{1-3} hydroxyalkyl, -$(CH_2)_{0-2}$-C_{3-5} heterocycloalkyl, -$(CH_2)_{1-2}$-O-C_{3-5} heterocycloalkyl, -methylene-C(=O)-$NR_{10}R_{11}$, or -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$; wherein the -$(CH_2)_{0-2}$-C_{3-5} heterocycloalkyl or the -$(CH_2)_{1-2}$-O-C_{3-5} heterocycloalkyl of R_{12} is optionally substituted with -C_{1-4} alkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, -$(CH_2)_{0-1}$-phenyl, halogen, -C_{1-3} fluoroalkyl, or -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl; wherein the -C_{1-3} alkyl of R_{12} is optionally substituted with one, two, or three of oxo or $NR_{10}R_{11}$;

R_{12A} is H or -C_{1-4} alkyl; or

R_{12} and R_{12A} form a C_{3-10} heterocycle optionally substituted with one, two, or three of -OH, -C_{1-3} alkyl, oxo, halogen, -C_{2-3} oxoalkyl, -C_{1-3} alkoxy, -C_{1-3} hydroxyalkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, cyano, -C_{3-6} cycloalkyl, -$S(=O)_2CH_3$, -$S(=O)_2CH_2CH_3$, -$C(=O)$-$NR_{10}R_{11}$, or -$NHC(=O)CH_3$;

R_{13} is H, -C_{1-6} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{1-3} alkyl-C_{1-3} alkoxy, -C_{1-4} cyanoalkyl, -C_{0-1} alkylene-C_{3-5} cycloalkyl, -C_{2-4} oxoalkyl, or -C_{0-1} alkylene-C_{3-5} heterocycloalkyl; wherein the -C_{1-6} alkyl of R_{13} is optionally substituted with one, two, or three of oxo, fluoro, -NH_2, C_{3-6} cycloalkyl, or methoxy; wherein the -C_{3-5} cycloalkyl or the -C_{3-6} cycloalkyl of R_{13} is optionally substituted with one, two, or three of -C_{1-3} alkyl, -C_{1-3} fluoroalkyl, or halogen;

R_{14} is H; or

X_4 is NR_{13} and R_{13} and R_{14} form a C_{4-5} heterocycle fused to Ring C;

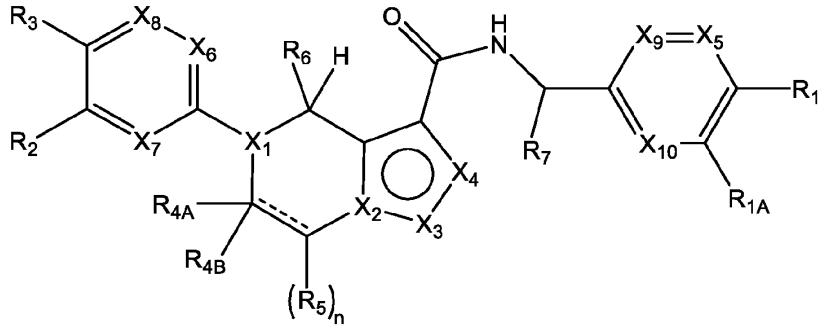
n is 1 or 2;

m is 0 or 1;

wherein if X_3 is CR_{13} or NR_{13} then X_4 is CH or N, and if X_4 is NR_{13} then X_3 is N, O, or S;

wherein the respective heterocycles each independently include 1 to 4 heteroatoms including at least one of N, O, or S.

2. A compound of Formula IA, or a pharmaceutically acceptable salt thereof, that is optionally a compound of Claim 1:



IA

wherein

X_1 is CH, CNH_2, or N;

X_2 is C or N;

X_3 is CR_{13}, N, NR_{13}, O, or S;

X_4 is CH, N, or NR_{13};

X_5 is CH, CR_{1B}, or N;

X_6 is CH or N;

X_7 is CH, N, or CF;

X_8 is CH or N;

X_9 is CH, CR_{1B}, or N;

X_{10} is CH, CR_{1B}, or N;

R_1 is $-NHR_8$, -OH, $-C_{2-5}$ heterocycle, or $-C_{1-3}$ alkyl; wherein the $-C_{2-5}$ heterocycle of R_1 is optionally substituted with one, two, or three of $-C_{1-3}$ alkyl, $-C_{1-3}$ oxoalkyl, $-C_{3-5}$ heterocycloalkyl, $-C_{3-5}$ hydroxyheterocycloalkyl, $-C_{3-5}$ aminoheterocycloalkyl, or oxo; wherein the $-C_{1-3}$ alkyl of R_1 is optionally substituted with one, two, or three of oxo or $-NR_{10}R_{11}$;

R_{1A} is H or $-CH_3$; or

R_1 and R_{1A} form a C_{6-8} fused heterocycloalkyl or a C_{6-8} fused heteroaryl; wherein the C_{6-8} fused heterocycloalkyl or the C_{6-8} fused heteroaryl is optionally substituted with oxo;

each R_{1B} independently is H, $-CH_3$, F, Cl, or methoxy;

R_2 is H, $-C_{1-3}$ alkyl, $-C_{1-3}$ fluoroalkyl, or halogen;

R_3 is $-C_{1-3}$ alkyl, $-C_{2-10}$ heterocycle, or -NH-C(=O)-C_{1-3} alkyl; wherein the $-C_{1-3}$ alkyl of R_3 is optionally substituted with one or more of oxo, -OH, $-NR_{12}R_{12A}$, $-C_{5-8}$ heterocycle, or cyano; wherein the $-C_{2-10}$ heterocycle is optionally substituted with one, two, or three of -OH, halogen, $-C_{1-3}$ hydroxyalkyl, $-C_{1-3}$ alkyl, cyclopropyl, or oxo; or

R_2 and R_3 form a C_{6-10} fused heterocycle optionally substituted with one, two, or three of $-C_{1-3}$ alkyl, $-C_{2-3}$ oxoalkyl, or oxo;

R_{4A} is H, -OH, or $-C_{1-3}$ alkyl;

R_{4B} is H or is absent;

each R_5 independently is H, halogen, -OH, cyclopropyl, or $-C_{1-3}$ alkyl; or two R_5 groups form cyclopropyl;

R_6 is H, -OH, or $-C_{1-3}$ alkyl; or

R_{4A} and R_6 or R_5 and R_6 form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge;

R_7 is H, $-C_{1-3}$ alkyl, or $-C_{1-3}$ hydroxyalkyl;

R_8 is H, $-C_{1-3}$ alkyl, $-SO_2CH_3$, or a $-C_{3-4}$ heterocycle; wherein the $-C_{1-3}$ alkyl of R_8 is optionally substituted with one, two, or three of oxo, $-C_{3-7}$ heterocycloalkyl, $-C_{3-7}$ heterocycloalkyl substituted with methyl, alkoxy, cyanoimine, or $-NR_9R_{10}$; wherein the $-C_{3-4}$ heterocycle is optionally substituted with one, two, or three of oxo, halogen, $-C_{0-1}$ alkylene-$NR_{10}R_{11}$, -OH, $-C_{1-3}$ hydroxyalkyl, $-C_{1-3}$ alkoxy optionally substituted with $-NR_{10}R_{11}$, $-C_{1-3}$ alkoxy-C_{1-3} alkyl, $-C_{1-3}$ oxoalkyl, or $-C_{1-3}$ alkyl;

R_9 is H, $-C_{1-4}$ alkyl, $-C_{1-4}$ hydroxyalkyl, $-C_{1-3}$ fluoroalkyl, $-C_{3-5}$ cycloalkyl, or $-C_{3-5}$ heterocycloalkyl; wherein the $-C_{1-4}$ alkyl of R_9 is optionally substituted with one, two, or three of cyclopropyl, $-C_{3-5}$ heterocycloalkyl, or methoxy; wherein the $-C_{3-5}$ cycloalkyl of R_9 is optionally substituted with $-C_{1-3}$ alkyl;

each R_{10} independently is H or $-C_{1-4}$ alkyl; or

if the $-C_{1-3}$ alkyl of R_8 is substituted with $-NR_9R_{10}$, then the corresponding R_9 and R_{10} are optionally combined to form a C_{3-7} heterocycloalkyl optionally substituted with one, two, or three of methoxy, -OH, $-C_{1-3}$ alkyl, halogen, $-NH_2$, $-NHCH_3$, or $-N(CH_3)_2$;

each R_{11} independently is H or $-C_{1-3}$ alkyl;

R_{12} is H, -C_{1-3} alkyl, -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl, or -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$; wherein the -$(CH_2)_{0-1}$-C_{3-5} heterocycloalkyl is optionally substituted with -C_{1-4} alkyl;

R_{12A} is H or -C_{1-4} alkyl; or

R_{12} and R_{12A} form a fused C_{5-10} heterocycloalkyl optionally substituted with -C_{1-3} alkyl;

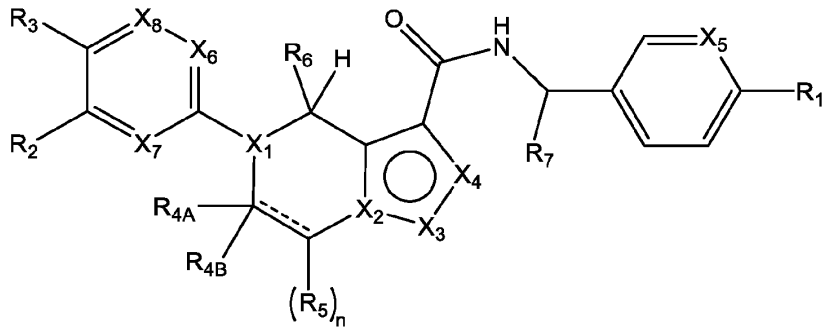
R_{13} is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{0-1}-C_{3-5} cycloalkyl, -C_{2-4} oxoalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_{13} is optionally substituted with one, two, or three of cyclopropyl or methoxy; wherein the -C_{3-5} cycloalkyl of R_{13} is optionally substituted with -C_{1-3} alkyl;

n is 1 or 2;

wherein the respective heterocycles each independently include 1 to 3 heteroatoms including at least one of N, O, or S;

wherein at least one of X_2 is N or X_3 is N, NH, or NR_{13}, and X_4 is N or NR_{13}; or if X_3 is S or O, then X_2 is C.

3. A compound of Formula IB or a pharmaceutically acceptable salt thereof, that is optionally a compound of Claim 1 or Claim 2:



IB

wherein

X_1 is CH, CNH_2, or N;

X_2 is C or N;

X_3 is CR_{13}, N, NR_{13}, O, or S;

X_4 is CH, N, or NR_{13};

X_5 is CH or N;

X_6 is CH or N;

X_7 is CH, N, or CF;

X_8 is CH or N;

with the proviso that at least one of X_2 is N or X_3 is N, NH, or NR_{13}, and X_4 is N or N R_{13}; or if X_3 is S or O, then X_2 is C;

R_1 is -NHR_8, -OH, -C_{2-5} heterocycle, or -C_{1-3} alkyl; wherein the -C_{2-5} heterocycle of R_1 is optionally substituted with one or more of -C_{1-3} alkyl, -C_{1-3} oxoalkyl, -C_{3-5} heterocycloalkyl, -C_{3-5}

hydroxyheterocycloalkyl, -C_{3-5} aminoheterocycloalkyl, or oxo; wherein the -C_{1-3} alkyl of R_1 is optionally substituted with one or more of oxo or -$NR_{10}R_{11}$;

R_2 is H, -C_{1-3} alkyl, -C_{1-3} fluoroalkyl, or halogen;

R_3 is -C_{1-3} alkyl, -C_{2-10} heterocycle, or -NH-C(=O)-C_{1-3} alkyl; wherein the -C_{1-3} alkyl of R_3 is optionally substituted with one or more of oxo, -OH, -$NR_{12}R_{12A}$, -C_{5-8} heterocycle, or cyano; wherein the -C_{2-10} heterocycle is optionally substituted with one or more of -OH, halogen, -C_{1-3} hydroxyalkyl, -C_{1-3} alkyl, cyclopropyl, or oxo; or

R_2 and R_3 form a C_{6-10} fused heterocycloalkyl optionally substituted with one or more of -C_{1-3} alkyl, -C_{2-3} oxoalkyl, or oxo;

R_{4A} is H, -OH, or -C_{1-3} alkyl;

R_{4B} is H or is absent;

each R_5 independently is H, -OH, halogen, or -C_{1-3} alkyl; or two R_5 groups form cyclopropyl;

R_6 is H, -OH, or -C_{1-3} alkyl; or

R_{4A} and R_6 or R_5 and R_6 form a C_{1-3} alkyl bridge or a C_{1-3} heteroalkyl bridge;

R_7 is H, -C_{1-3} alkyl, or -C_{1-3} hydroxyalkyl;

R_8 is H, -C_{1-3} alkyl, or a -C_{3-4} heterocycle; wherein the -C_{1-3} alkyl of R_8 is optionally substituted with one or more of oxo or -NR_9R_{10}; wherein the -C_{3-4} heterocycle is optionally substituted with one or more of oxo or -C_{1-3} alkyl;

R_9 is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_9 is optionally substituted with one or more of cyclopropyl, -C_{3-5} heterocycloalkyl, or methoxy; wherein the -C_{3-5} cycloalkyl of R_9 is optionally substituted with -C_{1-3} alkyl;

each R_{10} independently is H or -C_{1-4} alkyl; or

if the -C_{1-3} alkyl of R_8 is substituted with -NR_9R_{10}, then the corresponding R_9 and R_{10} are optionally combined to form a C_{3-6} heterocycloalkyl optionally substituted with at least one of methoxy, -OH, -C_{1-3} alkyl, or -$N(CH_3)_2$;

each R_{11} independently is H or -C_{1-3} alkyl;

R_{12} is H, -C_{1-3} alkyl, or -methylene-phenylene-NH-C(=O)-$NR_{10}R_{11}$;

each R_{13} independently is H, -C_{1-4} alkyl, -C_{1-4} hydroxyalkyl, -C_{1-3} fluoroalkyl, -C_{3-5} cycloalkyl, or -C_{3-5} heterocycloalkyl; wherein the -C_{1-4} alkyl of R_{13} is optionally substituted with one or more of cyclopropyl or methoxy; wherein the -C_{3-5} cycloalkyl of R_{13} is optionally substituted with -C_{1-3} alkyl;

n is 1 or 2;

wherein the respective heterocycles each independently include 1 to 3 heteroatoms including at least one of N, O, or S;

wherein at least one of X_2 is N or X_3 is N, NH, or NR_{13}, and X_4 is N or NR_{13}; or if X_3 is S or O, then X_2 is C.

4. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_3 is -C_{1-3} alkyl or -C_{2-10} heterocycle; wherein the -C_{2-10} heterocycle is -C_{2-5} heteroaryl; wherein the -C_{1-3} alkyl of R_3 is optionally substituted with one, two, or three of oxo or -$NR_{12}R_{12A}$; wherein the -C_{2-5} heterocycle of R_3 is optionally substituted with -C_{1-3} alkyl.

5. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_1 is -NHR_8; and R_8 is -C_{1-3} alkyl substituted with one, two, or three of oxo or -NR_9R_{10}.

6. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_2 is H; and R_3 is -C_{1-3} alkyl substituted with oxo and -$NR_{12}R_{12A}$.

7. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of: X_5 is CH; X_7 is CH or N; X_8 is CH; R_1 is -NHR_8, -C_{2-5} heterocycle, or -C_{1-3} alkyl; R_{4A} is H or -C_{1-3} alkyl; each R_5 independently is H, halogen, or -C_{1-3} alkyl; or the two R_5 groups form cyclopropyl; R_6 is H or -C_{1-3} alkyl; or R_7 is H or -C_{1-3} alkyl.

8. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_3 is -C_{1-3} alkyl substituted with oxo and -$NR_{12}R_{12A}$ and R_1 is -NHR_8 or -C_{1-3} alkyl substituted with oxo and -$NR_{10}R_{11}$.

9. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X_3 is CR_{13} and X_4 is CH or N.

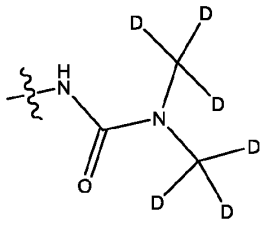
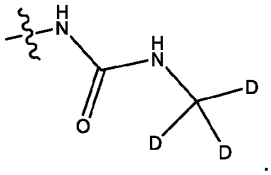
10. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_1 is -NHR_8; wherein R_8 is -C_{1-3} alkyl or a -C_{3-4} heterocycle; wherein the -C_{1-3} alkyl of R_8 is substituted with oxo and -NR_9R_{10}; wherein the -C_{3-4} heterocycle is substituted with one, two, or three of oxo or -C_{1-3} alkyl.

11. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X_1 is N, X_3 is N or NR_{13}, and X_4 is N.

12. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein the -C_{2-10} heterocycle of R_3 is a -C_{2-5} heterocycle and R_3 is optionally substituted with one, two, or three of -C_{1-3} alkyl.

13. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one hydrogen is deuterium.

14. The compound of Claim 13, or a pharmaceutically acceptable salt thereof,

wherein R_1 is  or .

15. The compound of Claim 13 or 14, or a pharmaceutically acceptable salt thereof, wherein R_{1A} is deuterium; X_5, X_9, and X_{10} are each CR_{1B}; and the R_{1B} of each of X_5, X_9, and X_{10} is deuterium.

16. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is one of:

N-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-N-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-c]pyridine-3-carboxamide; or

5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

17. A compound, wherein the compound is one of :

N-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-5-(5-(2-oxopyrrolidin-1-yl)pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

5-(5-(6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyridine-6-carbonyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

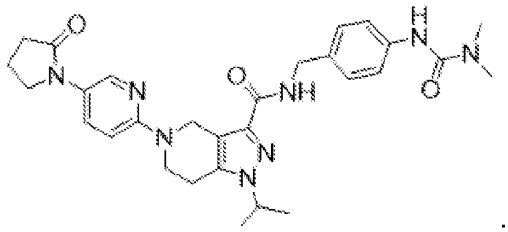
5-(5-(Dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1,7-dimethyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

(*S*)-5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-isopropyl-7-methyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide;

(*S*)-5-(4-(dimethylcarbamoyl)phenyl)-1-isopropyl-7-methyl-N-(4-(4-methylpiperazine-1-carboxamido)benzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide; or

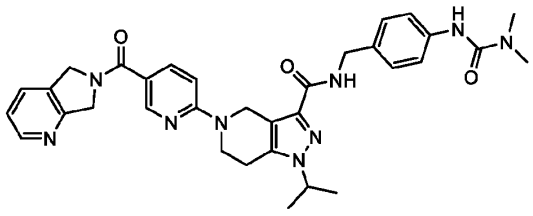
5-(5-(dimethylcarbamoyl)pyridin-2-yl)-*N*-(4-(3,3-dimethylureido)benzyl)-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*c*]pyridine-3-carboxamide.

18. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is

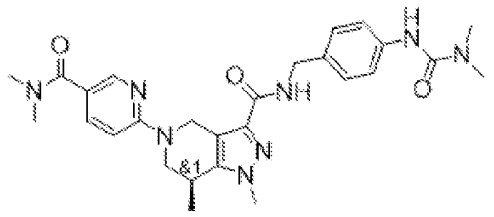


19. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is

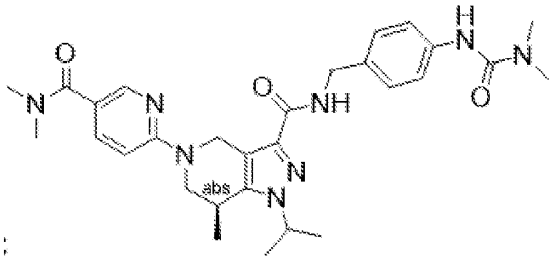
20. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is



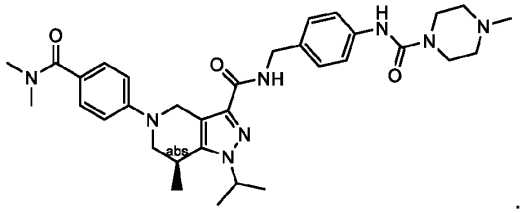
21. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is



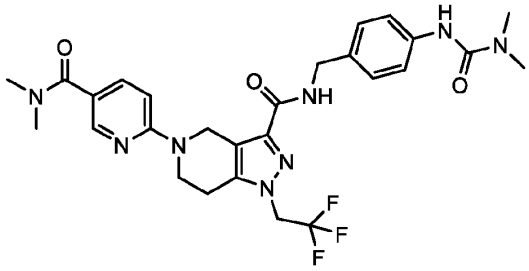
22. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is



23. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is



24. A compound or a pharmaceutically acceptable salt thereof; wherein the compound is



25. A pharmaceutical composition comprising the compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

26. A method for treating atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease, chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa comprising administering to a subject in need thereof a therapeutically effective amount of the compound of any of claims 1 to 24, or a pharmaceutically acceptable salt thereof.

27. A method for treating at least one of a dermatological condition or a respiratory condition comprising administering to a subject in need thereof a therapeutically effective amount of the compound of any of claims 1 to 24, or a pharmaceutically acceptable salt thereof.

28. A compound according to any of claims 1 to 24, or a pharmaceutically acceptable salt thereof, for use as a medicament.

29. A compound according to any of claims 1 to 24, or a pharmaceutically acceptable salt thereof, for use in the treatment of atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic obstructive pulmonary disease (COPD), chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), a joint disorder, keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa.

30. A compound according to any of claims 1 to 24, or a pharmaceutically acceptable salt thereof, for use in the treatment of at least one of a dermatological condition or a respiratory condition.

31. Use of a compound according to any of claims 1 to 24, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of atopic dermatitis, eosinophilic gastritis, atopic keratoconjunctivitis, allergy, alopecia, Alzheimer's disease, asthma, atherosclerosis, Bechet's disease, bullous pemphigoid, cancer, chronic

obstructive pulmonary disease (COPD), chronic pruritis, chronic urticaria, Crohn's disease (CD), dermatitis, diabetic kidney disease, eosinophilic esophagitis, fungal keratitis, gout, idiopathic pulmonary fibrosis (IPF), a joint disorder, keloids, non-alcoholic steatohepatitis (NASH), primary biliary cirrhosis, prurigo nodularis, psoriasis, psoriatic arthritis, rhinosinusitis, scleroderma, systemic lupus erythematosus (SLE), systemic sclerosis, ulcerative colitis (UC), vitiligo, or hidradenitis suppurativa.

32. Use of a compound according to any of claims 1 to 24, or a pharmaceutically acceptable salt thereof, for use in the treatment of at least one of a dermatological condition or a respiratory condition.