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(71) Applicant: **ADURO BIOTECH, INC.** [US/US]; 740 Heinz Avenue, Berkeley, California 94710 (US).

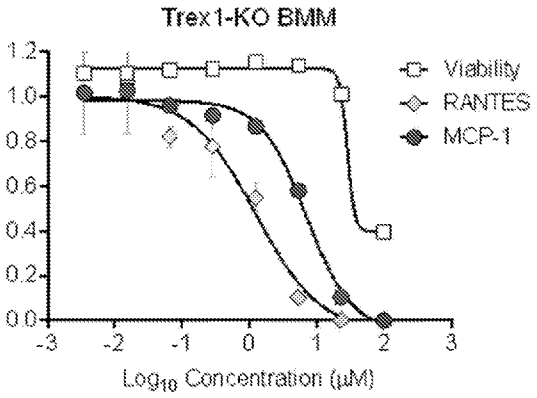
(72) Inventors: **NDUBAKU, Chudi Obioma**; 6031 Chabolyn Terrace, Oakland, California 94618 (US). **KATIBAH, George Edwin**; 34812 Candice Court, Fremont, California 94555 (US). **ROBERTS, Tucker Curran**; 2701 Prince St. Apt. 3, Berkeley, California 94705 (US). **SUNG, Leonard**; 25 Rolling Hills Avenue, San Mateo, California 94403 (US). **CIBLAT, Stephane**; 607-408 rue Saint Jacques, Montreal, Québec H2Y 1S2 (CA). **RAEPPEL, Franck**; 3194 Rue Claude-Jodoin, Montreal, Québec H1Y 3M2 (CA). **LY, Vu Linh**; 7524 rue Berri, Montreal, Québec H2R 2G7 (CA). **RAMTOHUL, Yeeman K.**; 12665 Boul Gouin Ouest, Pierrefonds, Québec H8Z 1W6 (CA). **RYBAK, Taras**; 1548 Rue Basin, Montreal, Québec H3C 0L4 (CA). **ZAKY, Mariam**; 1 Nassau Street, Apt 515, Boston MA, 02111 (US). **GILLARD, Laura**; 14-2645 Rue Beaubien Est, Montreal, Québec H1Y 1G6 (CA). **ISMAILI, Hossein**; 1000 Montee du Bois-Franc, Tres-Saint-Redempteur, Québec J0P 1P1 (CA).

(74) Agent: **ERLACHER, Heidi A.** et al.; Cooley LLP, 1299 Pennsylvania Avenue, NW, Suite 700, Washington, District of Columbia 20004 (US).

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(54) Title: PYRAZOLOPYRIMIDINONE COMPOUNDS AND USES THEREOF

FIG. 1



(57) Abstract: The present invention relates to pyrazolopyrimidinone compounds. The present invention also relates to pharmaceutical compositions containing these compounds and methods of treating autoimmune, inflammatory, and neurodegenerative diseases by administering these compounds and pharmaceutical compositions to subjects in need thereof. The present invention also relates to the use of such compounds for research or other non-therapeutic purposes.

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[Continued on next page]

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PYRAZOLOPYRIMIDINONE COMPOUNDS AND USES THEREOF

RELATED APPLICATIONS

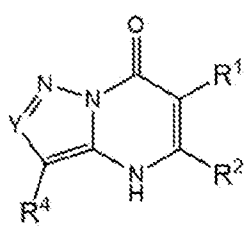
[0001] This application claims priority to, and the benefit of, U.S. Provisional Application Nos. 62/559,482, filed on September 15, 2017; 62/633,248, filed on February 21, 2018; and 62/687,769, filed on June 20, 2018, the contents of each of which are incorporated herein by reference in their entirety.

BACKGROUND

[0002] The enzyme cyclic GMP-AMP Synthase (cGAS) catalyzes the synthesis of cyclic GMP-AMP (cGAMP) from ATP and GTP in the presence of DNA. This cGAMP then functions as a second messenger that binds to and activates STimulator of INterferon Genes (STING). The activation of IRF3 and the NF-κB signaling by this pathway results in the production of cytokines and type I interferons, which triggers an innate immune response to bacterial or viral infection. Genetic mutations that alter the balance of this pathway may result in an increased activation of the STING pathway, resulting in autoimmune and inflammatory diseases. For example, a loss of function mutation of TREX1 exonuclease, which digests DNA, can result in an accumulation of self-DNA in the cytosol, leading to excessive levels of cGAMP produced by cGAS and elevated expression of interferon induced genes in this pathway. Mutations in TREX1 are associated with systemic inflammatory diseases such as Aicardi-Goutieres Syndrome, familial chilblain lupus and systemic lupus erythematosus. *Trex*$^{-/-}$ mice were shown to exhibit autoimmune and inflammatory phenotypes which are eliminated with genetic deletion of *cGas* in these mice (Gao et al., PNAS 112(42):E5699-705, 2015; Gray et al., The Journal of Immunology 195:1939-1943, 2015). Thus there is a need for inhibitors of the cGAS/STING pathway for the treatment of a variety of diseases.

SUMMARY

[0003] The present invention provides the compounds of Formula (I):



(I),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In this formula:

Y is $-CR^3=$ or $-N=$;

R^1 is Q^1-T^1-$(X^1)_n$;

Q^1 is a bond or C_{1-3}alkylene, wherein the C_{1-3}alkylene group is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w2}$, and $-NR^{w2}R^{x2}$;

T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, $-C(=O)C_{0-3}$alkylene-C_{3-8}cycloalkyl, $-C(=O)$-C_{0-3}alkylene-C_{6-10}aryl, $-C(=O)$-C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, $-C(=O)$-C_{0-3}alkylene-5 to 10-membered heteroaryl, $-NR^aR^b$, $-S(=O)_2R^a$, $-NR^aC(=O)R^a$, $-NR^aC(=O)NR^aR^b$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^a$, $-C(=O)NR^aS(=O)_2R^a$, $-NR^aS(=O)_2NR^aR^b$, $-C(=O)NR^aR^b$, or $-S(=O)_2NR^aR^b$;

each X^1 is independently selected from the group consisting of halo, cyano, oxo, C_{0-3}alkylene-$C(=O)R^c$, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-$C(=O)OR^c$, C_{0-3}alkylene-$OC(=O)R^c$, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$N^+R^cR^dR^{d'}$, C_{0-3}alkylene-$S(=O)_mR^c$, C_{0-3}alkylene-$NR^cC(=O)R^c$, C_{0-3}alkylene-$NR^cC(=O)NR^cR^d$, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=O)OR^c$, C_{0-3}alkylene-$NR^cS(=O)_2R^c$, C_{0-3}alkylene-$C(=O)NR^cS(=O)_2R^c$, C_{0-3}alkylene-$NR^cS(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=O)NR^cR^d$, C_{0-3}alkylene-$S(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, and R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S1} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, nitro, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$NR^eC(=O)R^e$, C_{0-3}alkylene-$NR^eC(=O)OR^e$, C_{0-3}alkylene-$NR^eC(=O)NR^eR^f$, C_{0-3}alkylene-$OC(=O)R^e$, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-3}alkylene-$C(=O)NR^eR^f$, C_{0-3}alkylene-$C(=O)R^e$, C_{0-3}alkylene-$S(=O)_mR^e$, C_{0-3}alkylene-$S(=O)_2NR^eR^f$, C_{0-3}alkylene-$NR^eS(=O)_2R^e$, C_{0-3}alkylene-$C(=O)NR^eS(=O)_2R^e$, C_{0-3}alkylene-$NR^eS(=O)_2NR^eR^f$, and R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl,

and each R^{S2} is optionally substituted with one or more substituents independently

selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^w, and -NR^wR^x;

R^2 is Q^2-T^2-$(X^2)_p$;

Q^2 is a bond or C_{1-3}alkylene, wherein the C_{1-3}alkylene group is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w3}, and -$NR^{w3}R^{x3}$;

T^2 is H, halo, cyano, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, -C(=O)-C_{0-3}alkylene-C_{3-8}cycloalkyl, -C(=O)-C_{0-3}alkylene-C_{6-10}aryl, -C(=O)-C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, -C(=O)-C_{0-3}alkylene-5- to 10-membered heteroaryl, -OR^z, -$S(=O)_mR^k$, -$P(=O)R^{kk}R^{mm}$, -NR^kR^m, -$C(=O)OR^k$, or -$C(=O)NR^kR^m$;

each X^2 is independently selected from the group consisting of halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-$C(=O)OR^n$, and R^{S3}, in which R^{S3} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and R^{S3} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^p, C_{0-3}alkylene-$S(=O)_mR^p$, C_{0-3}alkylene-NR^pR^q, C_{0-3}alkylene-$C(=O)NR^pR^q$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^p$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S4}, in which R^{S4} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S4} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w4}, and -$NR^{w4}R^{x4}$;

R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, -CN, -OR^r, -$C(=O)R^r$, -$S(=O)_mR^r$, NR^rR^t, or -$C(=O)OR^r$, wherein C_{1-3}alkyl, C_{2-3}alkenyl and C_{2-3}alkynyl are optionally substituted with one C_{3-6}cycloalkyl;

R^4 is C_{1-6}alkyl, C_{1-6}haloalkyl, $S(=O)_mR^u$, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl, wherein C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano,

C_{1-6}haloalkyl, OR^{w5}, and $NR^{w5}R^{x5}$;

each of R^a and R^b, independently, is H or R^{S5}, in which R^{S5} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and R^{S5} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, C_{0-3}alkylene-$OC(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)NR^{c2}R^{d2}$, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-$S(=O)_2NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$C(=O)NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2NR^{c2}R^{d2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S6} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{e2}R^{f2}$, C_{0-3}alkylene-OR^{e2}, C_{0-3}alkylene-$NR^{e2}C(=O)R^{e2}$, C_{0-3}alkylene-$NR^{e2}C(=O)OR^{e2}$, C_{0-3}alkylene-$NR^{e2}C(=O)NR^{e2}R^{f2}$, C_{0-3}alkylene-$OC(=O)R^{e2}$, C_{0-3}alkylene-$C(=O)OR^{e2}$, C_{0-3}alkylene-$C(=O)NR^{e2}R^{f2}$, C_{0-3}alkylene-$C(=O)R^{e2}$, C_{0-3}alkylene-$S(=O)_mR^{e2}$, C_{0-3}alkylene-$S(=O)_2NR^{e2}R^{f2}$, C_{0-3}alkylene-$NR^{e2}S(=O)_2R^{e2}$, C_{0-3}alkylene-$C(=O)NR^{e2}S(=O)_2R^{e2}$, C_{0-3}alkylene-$NR^{e2}S(=O)_2NR^{e2}R^{f2}$, and R^{S7}, in which R^{S7} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S7} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w6}, and -$NR^{w6}R^{x6}$;

each of R^c, R^{c2}, R^d, $R^{d'}$, and R^{d2}, independently, is H or R^{S8}, in which R^{S8} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S8} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{e3}R^{f3}$, C_{0-3}alkylene-OR^{e3}, C_{0-3}alkylene-$C(=O)OR^{e3}$, C_{0-3}alkylene-$C(=O)NR^{e3}R^{f3}$, C_{0-3}alkylene-$C(=O)R^{e3}$, C_{0-3}alkylene-$S(=O)_mR^{e3}$, C_{0-3}alkylene-$S(=O)_2NR^{e3}R^{f3}$, C_{0-3}alkylene-$NR^{f3}C(=O)R^{e3}$, C_{0-3}alkylene-$NR^{f3}S(=O)_mR^{e3}$, and

R^{S9}, in which R^{S9} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S9} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w7}, and -$NR^{w7}R^{x7}$;

each of R^{e}, R^{e2}, R^{e3}, R^{f}, R^{f2}, and R^{f3}, independently, is H or R^{S10}, in which R^{S10} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S10} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w8}, and -$NR^{w8}R^{x8}$;

each of R^{kk}, and R^{mm}, is independently selected from the group consisting of R^{k}, -OR^{k}, and -$NR^{k}R^{m}$;

each of R^{k}, and R^{m}, independently, is H or R^{z}, in which R^{z} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{z} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{n2}R^{o2}$, C_{0-3}alkylene-OR^{n2}, C_{0-3}alkylene-C(=O)OR^{n2}, C_{0-3}alkylene-C(=O)$NR^{n2}R^{o2}$, C_{0-3}alkylene-C(=O)R^{n2}, C_{0-3}alkylene-$S(=O)_mR^{n2}$, C_{0-3}alkylene-$S(=O)_2NR^{n2}R^{o2}$, and R^{S11}, in which R^{S11} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S11} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p2}, C_{0-3}alkylene-$S(=O)_mR^{p2}$, C_{0-3}alkylene-$NR^{p2}R^{q2}$, C_{0-3}alkylene-C(=O)$NR^{p2}R^{q2}$, C_{0-3}alkylene-C_{0-3}alkylene-C(=O)OR^{p2}, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S12}, in which R^{S12} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S12} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w9}, and -$NR^{w9}R^{x9}$;

each of R^{n}, R^{n2}, R^{o}, and R^{o2}, independently, is H or R^{S13}, in which R^{S13} is C_{1-6}alkyl,

C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S13} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p3}, C_{0-3}alkylene-$S(=O)_mR^{p3}$, C_{0-3}alkylene-$NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)OR^{p3}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S14}, in which R^{S14} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S14} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w10}$, and $-NR^{w10}R^{x10}$;

each of R^p, R^{p2}, R^{p3}, R^q, R^{q2}, and R^{q3}, independently, is H or R^{S15}, in which R^{S15} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S15} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w11}$, and $-NR^{w11}R^{x11}$;

each of R^r, R^t, and R^u, independently, is H or R^{S16}, in which R^{S16} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S16} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-C(=O)OR^{w12}$, $-OR^{w12}$, and $-NR^{w12}R^{x12}$;

each R^w, R^{w2}, R^{w3}, R^{w4}, R^{w5}, R^{w6}, R^{w7}, R^{w8}, R^{w9}, R^{w10}, R^{w11}, R^{w12}, R^x, R^{x2}, R^{x3}, R^{x4}, R^{x5}, R^{x6}, R^{x7}, R^{x8}, R^{x9}, R^{x10}, R^{x11}, and R^{x12}, independently, is H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl;

each of n and p independently is 0, 1, 2, 3, 4, or 5, wherein when T^2 is H, p is 0; and

m is 0, 1, or 2;

with the proviso that, for compounds where Y is $-CR^3=$:

a) when R^1 is unsubstituted phenyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl, unsubstituted phenyl, or unsubstituted pyridine;

b) when R^1 is unsubstituted cyclohexyl, R^2 is methyl and R^3 is methyl, R^4 is not unsubstituted pyridine;

c) when R^1 is unsubstituted cyclopentyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl or unsubstituted pyridine,

d) when R^2 is methyl, R^3 is methyl and R^4 is 3,4-di-ethoxy-phenyl, R^1 is not unsubstituted 1-pyrrolidine, unsubstituted 1-piperidine, 4-methyl-1-piperidine, 4-(phenylmethyl)-1-piperidine, unsubstituted 2-1,2,3,4-tetrahydro-isoquinoline, unsubstituted morpholine, or $NHCH_2CH_2$-3-indole;

e) when R^1 is unsubstituted CH_2-phenyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl, trifluoromethyl, 1-methyl-piperidin-4-yl, unsubstituted pyridine, unsubstituted phenyl, phenyl mono-substituted with 4-F, 4-Cl, 2-methoxy or 4-methoxy, or phenyl disubstituted with 3,4-methoxy;

f) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted pyridine, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 4-CN, 4-NO_2, 4-F or 2-F;

g) when R^2 is methyl, R^3 is methyl and R^4 is ethyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 4-CN or 4-NO_2;

h) when R^2 is methyl, R^3 is methyl and R^4 is 4-methoxy-phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 3-Cl, 4-Br, 2-methyl or 4-methyl;

i) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 3-Cl, 4-Cl, 4-Br, 2-methyl, 3-methyl, 4-methyl, 4-isopropyl or 4-*tert*-butyl; or R^1 is not unsubstituted CH_2-1-naphthylene or unsubstituted CH_2-pyridine;

j) when R^2 is methyl, R^3 is methyl and R^4 is 4-Cl-phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 4-Cl or 4-isopropyl;

k) when R^1 is unsubstituted CH_2-phenyl, R^2 is methyl and R^3 is trifluoromethyl, R^4 is not unsubstituted phenyl or phenyl substituted with 2-Cl or 4-Cl;

l) the compound is not wherein R^1 is CH_2-4-Br-phenyl, R^2 is methyl, R^3 is ethyl and R^4 is unsubstituted phenyl;

m) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not $CH_2CH_2C(=O)NH$-phenyl wherein the phenyl ring is unsubstituted or is substituted at the 4-position with Cl, methyl or methoxy;

n) when R^2 is methyl or ethyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not substituted pyrazolo[1,5-*a*]pyrimidin-7-yl;

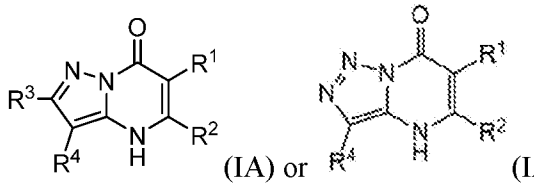
o) when R^2 is H, R^3 is isopropyl and R^4 is methyl, R^1 is not unsubstituted pyrazole; and

p) the compound is not wherein R^1 is unsubstituted CH_2-phenyl, R^2 is H, R^3 is methyl

and R^4 is unsubstituted phenyl; and

with the proviso that, for compounds where Y is -N=, the compound is not wherein R^1 is unsubstituted phenyl, R^2 is H and R^4 is 2-fluoro-phenyl.

[0004] For example, the compound can be of Formula (IA) or Formula (IA'):



(IA) or (IA').

[0005] For example, Q^1 is a bond or $-CH_2-$ and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, or $-C(=O)NR^aR^b$.

[0006] For example, Q^1 is a bond and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[0007] For example, Q^1 is a bond and T^1 is C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[0008] For example Q^1 is a bond and T^1 is phenyl, 5- or 6-membered monocyclic heteroaryl, or 9- or 10-membered bicyclic heteroaryl, preferabley wherein T^1 is 9- or 10-membered bicyclic heteroaryl.

[0009] For example, Q^1 is a bond or $-CH_2-$, T^1 is $-C(=O)NR^aR^b$ and n is 0.

[0010] For example, one of R^a and R^b is H or methyl and the other of R^a and R^b is not H or methyl.

[0011] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^n$, and each R^n and R^o is independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl.

[0012] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or OC_{1-6}alkyl.

[0013] For example, R^2 is H, cyano, methyl or methoxymethyl.

[0014] For example, R^2 is H, methyl or methoxymethyl.

[0015] For example, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, -CN, $-S(=O)_2C_{1-3}$alkyl or $-C(=O)OC_{1-3}$alkyl.

[0016] For example, R^3 is -CN, C_{1-3}alkyl, C_{1-3}haloalkyl or $-C(=O)OC_{1-3}$alkyl.

[0017] For example, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl or $-C(=O)OC_{1-3}$alkyl.

[0018] For example, R^3 is $-CF_3$, methyl or $-C(=O)OC_{1-3}$alkyl.

[0019] For example, R^3 is $-CF_3$ or -CN.

[0020] For example, R^3 is $-CF_3$

[0021] For example, R^3 is -CN.

[0022] For example, R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, $-S(=O)_2C_{1-3}$alkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$.

[0023] For example, R^4 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$, wherein Rw5 and Rx5 are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[0024] For example, R^4 is C_{3-8}cycloalkyl or C_{6-10}aryl, wherein C_{3-8}cycloalkyl and C_{6-10}aryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

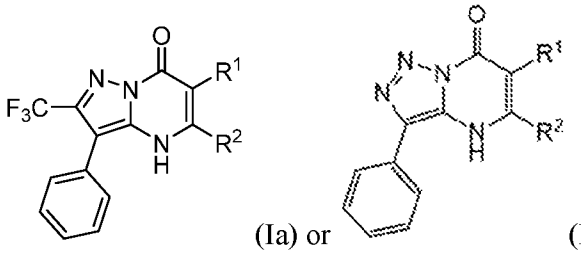
[0025] For example, R^4 is phenyl optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[0026] For example, R^4 is C_{3-8}cycloalkyl.

[0027] For example, R^4 is cyclopentyl.

[0028] For example, R^4 is phenyl.

[0029] For example, the compound can be of Formula (Ia) or Formula (Ia'):



(Ia) or (Ia').

[0030] For example, Q^1 is a bond or $-CH_2-$ and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, or $-C(=O)NR^aR^b$.

[0031] For example, Q^1 is a bond and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[0032] For example, Q^1 is a bond and T^1 is C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[0033] For example Q^1 is a bond and T^1 is phenyl, 5- or 6-membered monocyclic heteroaryl, or 9- or 10-membered bicyclic heteroaryl, preferabley wherein T^1 is 9- or 10-membered bicyclic heteroaryl.

[0034] For example, Q^1 is a bond or $-CH_2-$, T^1 is $-C(=O)NR^aR^b$ and n is 0.

[0035] For example, one of R^a and R^b is H or methyl and the other of R^a and R^b is not H or methyl.

[0036] For example, n is 0.

[0037] For example, T^1 is aryl or heteroaryl, preferably phenyl, 5- or 6-membered monocyclic heteroaryl, or 9- or 10-membered bicyclic heteroaryl.

[0038] For example, T^1 is 5- to 10-membered heteroaryl.

[0039] For example, T^1 is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indolinyl, isoindolyl, isoindolinyl, indazolyl, pyrazolopyridinyl, pyrazolopyrimidinyl, oxazolopyrimidinyl, oxazolopyridinyl, imidazopyridinyl, benzimidazolyl, tetrahydrobenzimidazolyl, benzofuranyl, dihydrobenzofuranyl, isobenzofuranyl, dihydroisobenzofuranyl, triazolopyridinyl, benzothiazolyl, azabenzimidazolyl, azabenzoxazolyl, azabenzothiazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, benzodioxolyl, chromanyl, tetrahydrooxazoloazepinyl, tetrahydrobenzoxazolyl, oxadiazolyl, thiadiazolyl, pyrazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl.

[0040] For example, T^1 is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, pyrazolopyridinyl, benzimidazolyl, benzothiazolyl, azabenzimidazolyl, azabenzoxazolyl, azabenzothiazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, oxadiazolyl, thiadiazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl.

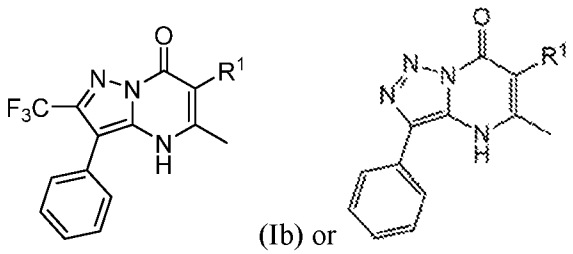
[0041] For example, T^1 is C_{0-1}alkylene-C_{6-10}aryl.

[0042] For example, T^1 is phenyl, benzyl, naphthyl, or CH_2naphthyl.

[0043] For example, T^1 is 3- to 12-membered heterocycloalkyl, preferably 4- to 10--membered heterocycloalkyl.

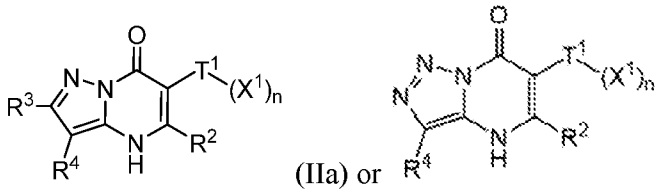
[0044] For example, T^1 is piperazine, piperidine, quinuclidine, or morpholine.

[0045] For example, the compound can be of Formula (Ib) or Formula (Ib'):



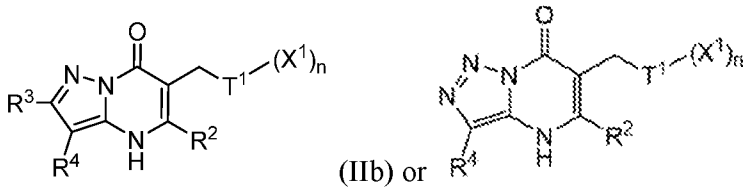
(Ib) or (Ib').

[0046] Subsets of compounds of Formula (I) includes those of Formula (IIa) or Formula (IIa'):



(IIa) or (IIa').

[0047] Subsets of compounds of Formula (I) includes those of Formula (IIb) or Formula (IIb'):

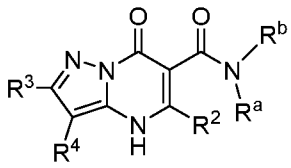
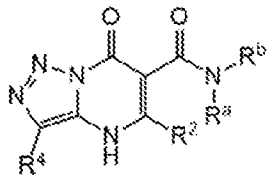


(IIb) or (IIb').

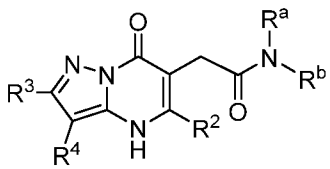
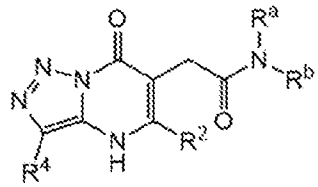
For example, T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, -C(=O)-C_{0-3}alkylene-C_{3-8}cycloalkyl, -C(=O)-C_{0-3}alkylene-C_{6-10}aryl, -C(=O)-C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, -C(=O)-C_{0-3}alkylene-5- to 10-membered heteroaryl, -NR^aR^b, -$S(=O)_2R^a$, -$NR^aC(=O)R^a$, -$NR^aC(=O)NR^aR^b$, -$NR^aC(=O)OR^a$, -$NR^aS(=O)_2R^a$, -$C(=O)NR^aS(=O)_2R^a$, -$NR^aS(=O)_2NR^aR^b$, -$C(=O)NR^aR^b$, or -$S(=O)_2NR^aR^b$; each X^1 independently is halo, cyano, oxo, C_{0-3}alkylene-$C(=O)R^c$, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, or R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5 to 10-membered heteroaryl, and R^{S1} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$NR^eC(=O)R^e$, C_{0-3}alkylene-$NR^eC(=O)OR^e$, C_{0-3}alkylene-$NR^eC(=O)NR^eR^f$, C_{0-3}alkylene-$OC(=O)R^e$, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-}

$_{3}$alkylene-C(=O)R^e, C_{0-3}alkylene-S(=O)$_m R^e$, C_{0-3}alkylene-S(=O)$_2 NR^eR^f$, C_{0-3}alkylene-$NR^eS(=O)_2R^e$, C_{0-3}alkylene-$NR^eS(=O)_2NR^eR^f$, and R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl, and R^{S2} is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^w, and -NR^wR^x.

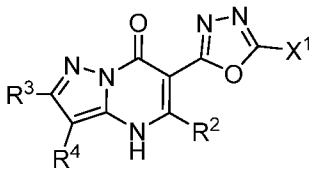
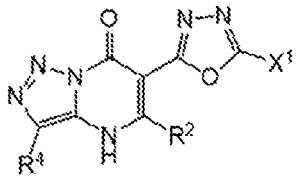
[0048] Subsets of compounds of Formula (I) includes those of Formula (IIc) or Formula (IIc'):


(IIc) or

(IIc').

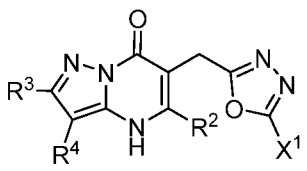
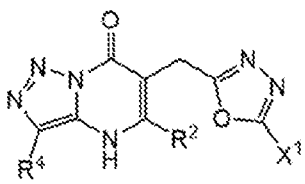
[0049] Subsets of compounds of Formula (I) includes those of Formula (IId) or Formula (IId'):


(IId) or

(IId').

[0050] Subsets of compounds of Formula (I) includes those of Formula (IIe) or Formula (IIe'):


(IIe) or

(IIe').

[0051] Subsets of compounds of Formula (I) includes those of Formula (IIf) or Formula (IIf'):


(IIf) or

(IIf').

[0052] For example, one of R^a and R^b independently is 5 to 10-membered heteroaryl and the other is hydrogen.

[0053] For example, one of R^a and R^b independently is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, benzimidazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl,

quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, oxadiazolyl, triazolyl, imidazolyl, furan, or thiophenyl, and the other of R^a and R^b is hydrogen.

[0054] For example, one of R^a and R^b is C_{0-1}alkylene-C_{6-10}aryl.

[0055] For example, one of R^a and R^b independently is phenyl, benzyl, naphthyl, or CH_2naphthyl.

[0056] For example, one of R^a and R^b independently is 5- to 9-membered heterocycloalkyl.

[0057] For example, one of R^a and R^b independently is dihydrobenzofuran, tetrahydrobenzimidazole, morpholine, tetrahydrofuran, piperidine, or piperazine.

[0058] For example, each of R^a and R^b independently is C_{5-6}cycloalkyl.

[0059] For example, each of R^a and R^b independently is cyclohexane or cyclopropane.

[0060] For example, X^1 is C_{0-1}alkylene-C_{6-10}aryl.

[0061] For example, X^1 is phenyl, benzyl, naphthyl, or CH_2naphthyl.

[0062] For example, X^1 is 5- to 10-membered heteroaryl.

[0063] For example, X^1 is benzoxazolyl, benzimidazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, oxadiazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl.

[0064] For example, X^1 is 5- to 9-membered heterocycloalkyl.

[0065] For example, X^1 is tetrahydrobenzoxazole, tetrahydrobenzimidazole, morpholine, tetrahydrofuran, tetrahydropyran, piperidine, pyrrolidine, or piperazine.

[0066] For example, X^1 is C_{3-6}cycloalkyl.

[0067] For example, X^1 is OR^a or $C(=O)C_{1-6}$alkyl.

[0068] For example, X^1 is C_{1-3}alkyl.

[0069] For example, X^1 is OCF_3, O C_{1-3}alkyl, NH_2, CN, OH or halo.

[0070] For example, X^1 is C_{0-1}alkylene-$C(=NR^c)NR^cR^d$.

[0071] For example, X^1 is C_{0-1}alkylene-$NR^cC(=NR^c)NR^cR^d$.

[0072] In one example, for a compound of Formula I, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof:

R^1 is Q^1-T^1-$(X^1)_n$;

Q^1 is a bond, -CH_2-, or -CH_2CH_2-;

T^1 is C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, -C(=O)-C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, -NR^aR^b, -$NR^aC(=O)R^a$, -$C(=O)NR^aS(=O)_2R^a$, or -$C(=O)NR^aR^b$;

each X^1 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-

$C(=O)OR^c$, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$N^+R^cR^dR^{d'}$, C_{0-3}alkylene-$S(=O)_mR^c$, C_{0-3}alkylene-$NR^cC(=O)R^c$, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-$C(=O)NR^cR^d$, C_{0-3}alkylene-$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, or R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl,

and each R^{S1} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, nitro, oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$NR^eC(=O)R^e$, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-3}alkylene-$C(=O)R^e$, C_{0-3}alkylene-$S(=O)_mR^e$, C_{0-3}alkylene-$NR^eS(=O)_2R^e$, and R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{6-10}aryl or C_{0-3}alkylene-3- to 12-membered heterocycloalkyl,

and each R^{S2} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^w$, and $-NR^wR^x$;

each of R^a and R^b, independently, is H or R^{S5}, in which R^{S5} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl,

and R^{S5} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-$NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, or C_{0-3}alkylene-3- to 12-membered heterocycloalkyl,

and each R^{S6} is optionally substituted with one or more substituents independently selected from the group consisting of C_{0-3}alkylene-C_{3-8}cycloalkyl C_{0-3}alkylene-$NR^{e2}R^{f2}$, C_{0-3}alkylene-OR^{e2};

R^2 is Q^2-T^2-$(X^2)_p$;

Q^2 is a bond, $-CH_2-$, or $-CH_2CH_2-$;

T^2 is H, halo, cyano, C_{1-6}alkyl, C_{3-8}cycloalkyl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, C(=O)- 3 to 12-membered heterocycloalkyl, $-OR^z$, $-S(=O)_mR^k$, $-P(=O)R^{kk}R^{mm}$, $-NR^kR^m$, $-C(=O)OR^k$ or $-C(=O)NR^kR^m$;

each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-$C(=O)OR^n$ or R^{S3}, in which R^{S3} is C_{1-6}alkyl optionally substituted with C_{0-3}alkylene-OR^p;

each of R^{kk}, and R^{mm}, is independently selected from the group consisting of R^k, -OR^k, and -NR^kR^m;

each of R^k, and R^m, independently, is H or R^z, in which R^z is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5 to 10-membered heteroaryl:

and each R^z is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{0-3}alkylene-$NR^{n2}R^{o2}$, C_{0-3}alkylene-OR^{n2}, C_{0-3}alkylene-$C(=O)OR^{n2}$, C_{0-3}alkylene-$C(=O)NR^{n2}R^{o2}$, and R^{S11}, in which R^{S11} is C_{0-3}alkylene-3 to 12-membered heterocycloalkyl,

and each R^{S11} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p2}, C_{0-3}alkylene-$S(=O)_mR^{p2}$, C_{0-3}alkylene-$NR^{p2}R^{q2}$, C_{0-3}alkylene-$C(=O)NR^{p2}R^{q2}$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^{p2}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and C_{1-6}haloalkyl;

R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, -CN, -OR^r, -$C(=O)R^r$, -$S(=O)_mR^r$, -NR^rR^t, or -$C(=O)OR^r$, wherein C_{1-3}alkyl, C_{2-3}alkenyl and C_{2-3}alkynyl are optionally substituted with C_{3-6}cycloalkyl;

R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl, wherein C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5 to 10-membered heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$;

each of R^c, R^{c2}, R^d, $R^{d'}$, and R^{d2}, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^e, R^{e2}, R^f, and R^{f2}, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^n, R^{n2}, R^o, and R^{o2}, independently, is H or R^{S13}, in which R^{S13} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl; and each R^{S13} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p3}, C_{0-3}alkylene-$S(=O)_mR^{p3}$, C_{0-3}alkylene-$NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)OR^{p3}$, C_{1-6}alkyl,

C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, and C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^p, R^{p2}, R^{p3}, R^{q2}, and R^{q3}, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^r, and R^t, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^w, R^{w5}, R^x, and R^{x5}, independently, is H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl;

each of n and p independently is 0, 1, 2, 3, 4, or 5, wherein when T^2 is H, p is 0; and m is 0, 1, or 2.

[0073] In one example, for a compound of Formula I, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof:

R^1 is -$(CH_2)_{0-1}$-C(=O)NR^aR^b; -CH_2CH_2-NR^aR^b; -CH_2CH_2-$NR^aC(=O)R^a$; -C(=O)$NR^aS(=O)_2R^a$; -$(CH_2)_{0-1}$-C_{6-10}aryl; -$(CH_2)_{0-1}$-5- to 6-membered monocyclic heteroaryl; -$(CH_2)_{0-1}$-9- to 10-membered bicyclic heteroaryl; a 4- to 6-membered monocyclic heterocycloalkyl; a 9- to 10-membered bicyclic heterocycloalkyl; -C(=O)-4- to 6-membered monocyclic heterocycloalkyl; -C(=O)-9- to 10-membered bicyclic heterocycloalkyl; wherein the aryl, 5heteroaryl, and heterocycloalkyl rings are optionally independently substituted with 1, 2, 3, 4, or 5 X^1;

each X^1 independently is halo; cyano; oxo; C_{1-6}alkyl optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-C(=O)OR^e, C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, and C_{0-3}alkylene-4 to 6-membered heterocycloalkyl, wherein heterocycloalkyl is optionally independently substituted with one or more C_{1-6}alkyl; C_{0-3}alkylene-C_{3-6}cycloalkyl optionally substituted with one or more substituents independently selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, and C_{0-3}alkylene-OR^e; C_{0-3}alkylene-C_{6-10}aryl, wherein C_{6-10}aryl is optionally substituted with one or more substituents selected from the group consisting of halo, cyano, nitro, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-C(=O)OR^e, C_{0-3}alkylene-C(=O)R^e, C_{0-3}alkylene-$S(=O)_mR^e$, and C_{0-3}alkylene-$NR^eS(=O)_2R^e$; C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl or 9- or 10-membered bicyclic heterocycloalkyl, wherein

heterocycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of oxo, C_{0-3}alkylene-NR^eR^f, and C_{0-3}alkylene-OR^e; C_{0-3}alkylene-5- or 6-membered monocyclic heteroaryl or 9- or 10-membered bicyclic heteroaryl, wherein heteroaryl is independently optionally substituted with one or more C_{0-3}alkylene-OR^e; C_{0-3}alkylene-OR^c; C_{0-3}alkylene-$C(=O)OR^c$; C_{0-3}alkylene-NR^cR^d; C_{0-3}alkylene-$N^+R^cR^dR^{d'}$; C_{0-3}alkylene-$S(=O)_mR^c$; C_{0-3}alkylene-$NR^cC(=O)R^c$; C_{0-3}alkylene-$OC(=O)NR^cR^d$; C_{0-3}alkylene-$C(=O)NR^cR^d$; C_{0-3}alkylene-$C(=NR^c)NR^cR^d$; or C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$;

each of R^a and R^b, independently, is H or R^{S5}, in which R^{S5} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl, C_{0-3}alkylene-9- or 10-membered bicyclic hetercycloalkyl, C_{0-3}alkylene-5- or 6-membered monocyclic heteroaryl, or C_{0-3}alkylene-9- or 10-membered bicyclic heteroaryl;

and R^{S5} is optionally substituted with one or more substituents selected from the group consisting of halo, cyano, oxo, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-$NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-6}cycloalkyl, or C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl;

and each R^{S6} is optionally substituted with one or more C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-$NR^{e2}R^{f2}$, C_{0-3}alkylene-OR^{e2};

R^2 is Q^2-T^2-$(X^2)_p$;

Q^2 is a bond, $-CH_2-$, or $-CH_2CH_2-$;

T^2 is H, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl, 4- to 6-membered monocyclic heterocycloalkyl, 9- or 10-membered bicyclic heterocycloalkyl, 5- or 6-membered monocyclic heteroaryl, 9- or 10-membered bicyclic heteroaryl, C(=O)- 4- to 6-membered monocyclic heterocycloalkyl, $-OR^z$, $-S(=O)_mR^k$, $-P(=O)R^kR^m$, $-NR^kR^m$, $-C(=O)OR^k$ or $-C(=O)NR^kR^m$;

each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-$C(=O)OR^n$ or C_{1-6}alkyl, wherein C_{1-6}alkyl is optionally substituted with one C_{0-3}alkylene-OR^p;

each of R^{kk}, and R^{mm}, is independently selected from the group consisting of R^k, $-OR^k$, and $-NR^kR^m$;

each of R^k, and R^m, independently, is H or R^z, in which R^z is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl, C_{0-3}alkylene-9- or 10-membered bicyclic heterocycloalkyl, C_{0-3}alkylene-5 or 6-membered monocyclic heteroaryl, or C_{0-3}alkylene-9- or 10-membered bicyclic heteroaryl:

and each R^z is optionally substituted with one or more substituents selected from the group consisting of halo, C_{1-6}alkyl, C_{0-3}alkylene-$NR^{n2}R^{o2}$, C_{0-3}alkylene-OR^{n2}, C_{0-3}alkylene-$C(=O)OR^{n2}$, C_{0-3}alkylene-$C(=O)NR^{n2}R^{o2}$, and R^{S11}, in which R^{S11} is C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl, C_{0-3}alkylene-9- or 10-membered bicyclic heterocycloalkyl, C_{0-3}alkylene-5- or 6-membered monocyclic heteroaryl, or C_{0-3}alkylene-9- or 10-membered bicyclic heteroaryl;

and each R^{S11} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p2}, C_{0-3}alkylene-$S(=O)_mR^{p2}$, C_{0-3}alkylene-$NR^{p2}R^{q2}$, C_{0-3}alkylene-$C(=O)NR^{p2}R^{q2}$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^{p2}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and C_{1-6}haloalkyl;

R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, -CN, $-OR^r$, $-C(=O)R^r$, $-S(=O)_mR^r$, NR^rR^t, or $-C(=O)OR^r$, wherein C_{1-3}alkyl, C_{2-3}alkenyl and C_{2-3}alkynyl are optionally substituted with C_{3-6}cycloalkyl;

R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, phenyl, or 5- or 6-membered monocyclic heteroaryl, wherein cycloalkyl, phenyl and heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$;

each of R^r, and R^t, independently, is H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, phenyl, 4- to 6-membered monocyclic heterocycloalkyl, or 5- or 6-membered monocyclic heteroaryl;

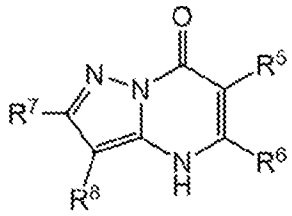
each of R^c, R^{c2}, R^d, $R^{d'}$, R^{d2}, R^e, R^{e2}, R^f, R^{f2}, R^n, R^{n2}, R^o, R^{o2}, R^p, R^{p2}, and R^{q2}, independently, is H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, phenyl, 4- to 6-membered monocyclic heterocycloalkyl, or 5- or 6--membered monocyclic heteroaryl;

each R^w, R^{w5}, R^x, and R^{x5}, independently, is H, C_{1-3}alkyl, or C_{1-3}haloalkyl;

p is 0, 1, 2, 3, 4, or 5; and

m is 0, 1, or 2.

[0074] In another aspect, the present invention provides the compounds of Formula (III):



(III),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In this formula:

R^5 is selected from the group consisting of $-C(=O)NR^9R^{10}$; $-CH_2C(=O)NR^{11}R^{12}$; $-CH_2CH_2NR^{13}R^{14}$; $-CH_2$-phenyl; $-CH_2$-5-membered monocyclic heteroaryl optionally substituted with one C_{1-3}alkyl, monocyclic C_{5-6}cycloalkyl, or phenyl, wherein phenyl is optionally substituted with one $-OC_{1-3}$alkyl; phenyl optionally substituted with one halo or C_{1-3}alkyl; a 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with 1, 2, or 3 R^{15}; a 5- or 6-membered monocylic heteroaryl optionally substituted with 1, 2, or 3 R^{16}; and 9- or 10-membered bicyclic heteroaryl optionally substituted with 1, 2, 3, or 4 R^{17};

R^9 and R^{10} are independently selected from the group consisting of H; C_{1-3}alkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH and $-OC_{1-3}$alkyl; $-CH_2$phenyl; $-S(=O)_2R^{18}$; C_{5-6}cycloalkyl optionally substituted with one $-NH_2$, oxo, -OH, or $-OC_{1-3}$alkyl; phenyl optionally substituted with 1, 2, or 3 R^{19}; a 5-or 6-membered monocyclic heterocycloalkyl optionally substituted with one $-C_{1-3}$alkyl, $-C(=O)C_{1-3}$alkyl, or $-C(=O)OC_{1-6}$alkyl; a 5- or 6-membered monocyclic heteroaryl optionally substituted with 1, 2, or 3 R^{20}; and a 9- or 10-membered bicyclic heteroaryl optionally substituted with 1 or 2 halo; or

R^9 and R^{10} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one phenyl;

R^{11} and R^{12} are independently selected from the group consisting of H; C_{1-3}alkyl optionally substituted with one -OH or $-OC_{1-3}$alkyl; phenyl optionally substituted with one $-NH_2$ or $-OC_{1-3}$alkyl; and a 5- or 6-membered monocyclic heteroaryl; or
R^{11} and R^{12} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one C_{1-3}alkyl, phenyl or $-CH_2$-phenyl, wherein the phenyl ring of phenyl or $-CH_2$-phenyl is optionally substituted with one C_{1-3}alkyl;

R^{13} and R^{14} are independently selected from the group consisting of H; $-C(=O)C_{1-3}$alkyl; -C(=O)phenyl; and phenyl optionally substituted with one $-OC_{1-3}$alkyl;

each R^{15} is independently selected from the group consisting of oxo; -C(=O)OH; -C(=O)OC_{1-3}alkyl; and C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl;

each R^{16} is independently selected from the group consisting of -CN; -C(=O)OH; -C(=O)OC_{1-3}alkyl; -C(=O)NH_2; -C(=O)NHC_{1-3}alkyl; -C(=O)N(C_{1-3}alkyl)$_2$; -C(=NH)NH_2; -NHC(=NH)NH_2; -NH_2; -NHC_{1-3}alkyl;-N(C_{1-3}alkyl)$_2$; -NHC_{3-6}cycoalkyl; -N(C_{1-3}alkyl)C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, or 5- or 6-membered monocyclic heterocycloalkyl, wherein the monocyclic heterocycloalkyl is optionally substituted with -C_{1-3}alkyl; C_{1-3}haloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH and phenyl; -C_{3-6}cycloalkyl optionally substituted with one -NH_2, C_{1-3}alkyl, C_{1-3}haloalkyl, or -OC_{1-3}alkyl; phenyl optionally substituted with one -OH, -OC_{1-3}alkyl, -NO_2, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of oxo, -OH, -NH_2, -OC_{1-3}alkyl, -C(=O)C_{1-3}alkyl, -S(=O)$_2C_{1-3}$alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OCH_2phenyl, and C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -NH_2, -NHS(=O)$_2C_{1-3}$alkyl, -OH, or -OC_{1-3}alkyl; and 5- or 6-membered monocyclic heteroaryl optionally substituted with one -OH or -OC_{1-3}alkyl;

each R^{17} is independently selected from the group consisting of oxo; halo; -OH; -CN; -NH_2; -NHC_{1-3}alkyl; -N(C_{1-3}alkyl)$_2$; -N^+(C_{1-3}alkyl)$_3$; -NHC(=O)C_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -S(=O)$_m$$C_{1-3}$alkyl; -C(=O)OH; -C(=O)O$C_{1-6}$alkyl; -C(=O)$NH_2$; -C(=O)NH$C_{1-3}$alkyl; -C(=O)N($C_{1-3}$alkyl)$_2$; -OC(=O)$NH_2$; -OC(=O)NH$C_{1-3}$alkyl; -OC(=O)N($C_{1-3}$alkyl)$_2$; -C(=NH)$NH_2$; -C(=NH)NH$C_{1-3}$alkyl; -C(=NH)N($C_{1-3}$alkyl)$_2$; -O$C_{1-3}$haloalkyl; C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; -OC_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, phenyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -C(=O)NH_2, -C(=O)NHC_{1-3}alkyl, -C(=O)N(C_{1-3}alkyl)$_2$, -NH_2, -NHC_{1-3}alkyl, -N(C_{1-3}alkyl)$_2$, -NHC(=O)C_{1-3}alkyl, or -NHS(=O)$_2C_{1-3}$alkyl; and phenyl optionally substituted with one halo, -CN, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl or -N(C_{1-3}alkyl)$_2$;

R^{18} is selected from the group consisting of C_{1-3}alkyl; monocyclic C_{3-6}cycloalkyl; a 5- or 6-membered monocyclic heteroaryl; phenyl; and -CH_2phenyl; wherein the phenyl ring of phenyl or -CH_2phenyl is optionally substituted with one halo, -CN, or -OC_{1-3}alkyl;

each R^{19} is independently selected from the group consisting of halo; -CN; -NH_2; -NHC_{1-3}alkyl; -$N(C_{1-3}alkyl)_2$; -NHC(=O)C_{1-3}alkyl; -NHS(=O)$_2C_{1-3}$alkyl; -$N(S(=O)_2C_{1-3}alkyl)_2$;-NHS(=O)$_2C_{3-6}$cycloalkyl; -NHS(=O)$_2$phenyl; -NHC(=O)OH; -NHC(=O)OC_{1-3}alkyl; -S(=O)$_2C_{1-3}$alkyl; -OC_{1-3}alkyl optionally substituted with one phenyl; C_{1-3}haloalkyl; -OC_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; a 5- or 6-membered monocyclic heterocycloalkyl; and C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -$N(C_{1-3}alkyl)_2$;

each R^{20} is independently selected from the group consisting of -CN; -OC_{1-3}alkyl; -S(=O)$_2C_{1-3}$alkyl; C_{1-3}haloalkyl; and C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl; and monocyclic C_{3-6}cycloalkyl;

R^6 is selected from the group consisting of H; halo; -CN; -NH_2; -C(=O)OH; -C(=O)OC_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -S(=O)$_m C_{1-3}$alkyl; -P(=O)$(C_{1-3}alkyl)_2$; -C(=O)$NR^{21}R^{22}$; C_{1-3}haloalkyl; -OC_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -$N(C_{1-3}alkyl)_2$; C_{1-3}alkyl optionally substituted with one -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)_2$, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -S(=O)$_m C_{1-3}$alkyl, -C(=O)C_{1-3}alkyl, -OR^{23}, or 5- or 6-membered monocyclic heteroaryl, wherein monocyclic heteroaryl is optionally substituted with 1 or 2 C_{1-3}alkyl; monocyclic C_{3-6}cycloalkyl optionally substituted with one -C(=O)OH, -C(=O)OC_{1-3}alkyl or C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -OH or -OC_{1-3}alkyl; a 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one -C(=O)OH, or -C(=O)OC_{1-3}alkyl; and a 5- or 6-membered heteroaryl optionally substituted with 1 or 2 C_{1-3}alkyl;

R^{21} and R^{22} are independently selected from the group consisting of H; C_{1-6}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)_2$, or 5- or 6-membered monocyclic heteroaryl; C_{1-3}haloalkyl optionally substituted with one -OH or -OC_{1-3}alkyl; a 5- or 6-membered monocyclic heteroaryl optionally substituted with 1 or 2 C_{1-3}alkyl; and a 4- to 6-membered monocyclic heterocycloalkyl; or

R^{21} and R^{22} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one -C(=O)OH, -C(=O)OC_{1-3}alkyl, or C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -OH or -OC_{1-3}alkyl;

R^{23} is selected from the group consisting of H; C_{1-3}haloalkyl; C_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -C(=O)NH_2, -C(=O)NHC_{1-3}alkyl, -C(=O)$N(C_{1-3}alkyl)_2$, phenyl, 5- or 6-membered monocyclic heteroaryl,

or 5- or 6-membered monocyclic heterocycloalkyl, wherein monocyclic heterocycloalkyl is optionally substituted with 1 or 2 oxo or C_{1-3}alkyl; a 4-, 5-, or 6-membered monocyclic heterocycloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of oxo and C_{1-3}alkyl; and a 5- or 6-membered monocyclic heteroaryl;

R^7 is selected from the group consisting of -CN; -OH; -C(=O)OH; -C(=O)OC_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -S(=O)$_m$$C_{1-3}$alkyl; -$NH_2$; -NH$C_{1-3}$alkyl; -N($C_{1-3}$alkyl)$_2$; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl; C_{1-3}haloalkyl; C_{2-3}alkenyl optionally substituted with one monocyclic C_{3-6}cycloalkyl; C_{2-3}alkyny optionally substituted with one monocyclic C_{3-6}cycloalkyl; monocyclic C_{3-6}cycloalkyl; -O-5- or 6-membered monocyclic heterocycloalkyl; and -OC_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, or -C(=O)OC_{1-3}alkyl;

R^8 is selected from the group consisting of C_{1-3}alkyl; C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; phenyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of -CN, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl and -OC_{1-3}haloalkyl; and pyridinyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of -CN, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl and -OC_{1-3}haloalkyl;

with the proviso that:

a) when R^5 is unsubstituted phenyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl, unsubstituted phenyl, or unsubstituted pyridine;

b) when R^5 is unsubstituted cyclohexyl, R^6 is methyl and R^7 is methyl, R^8 is not unsubstituted pyridine;

c) when R^5 is unsubstituted cyclopentyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl or unsubstituted pyridine,

d) when R^6 is methyl, R^7 is methyl and R^8 is 3,4-di-ethoxy-phenyl, R^5 is not unsubstituted 1-pyrrolidine, unsubstituted 1-piperidine, 4-methyl-1-piperidine, unsubstituted 2-1,2,3,4-tetrahydro-isoquinoline, or unsubstituted morpholine;

e) when R^5 is unsubstituted CH_2-phenyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl, trifluoromethyl, unsubstituted pyridine, unsubstituted phenyl, phenyl mono-substituted with 4-F, 4-Cl, 2-methoxy or 4-methoxy, or phenyl disubstituted with 3,4-methoxy;

f) when R^5 is unsubstituted CH_2-phenyl, R^6 is methyl and R^7 is trifluoromethyl, R^8 is not unsubstituted phenyl or phenyl substituted with 2-Cl or 4-Cl;

g) when R^6 is methyl, R^7 is methyl and R^8 is unsubstituted phenyl, R^5 is not $CH_2CH_2C(=O)NH$-phenyl wherein the phenyl ring is unsubstituted or is substituted at the 4-

position with Cl, methyl or methoxy;

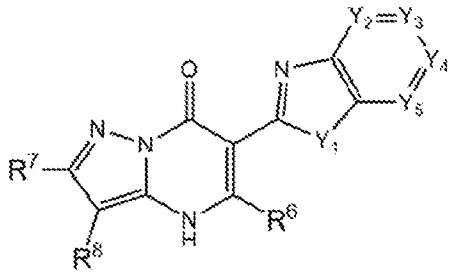
h) when R^6 is methyl or ethyl, R^7 is methyl and R^8 is unsubstituted phenyl, R^5 is not substituted pyrazolo[1,5-*a*]pyrimidin-7-yl;

i) when R^6 is H, R^7 is isopropyl and R^8 is methyl, R^5 is not unsubstituted pyrazole; and

j) the compound is not wherein R^5 is unsubstituted CH_2-phenyl, R^6 is H, R^7 is methyl and R^8 is unsubstituted phenyl.

[0075] In one embodiment of compounds of Formula (III), R^5 is a 9- or 10-membered bicyclic heteroaryl optionally substituted with 1, 2, 3, or 4 R^{17}.

[0076] In one embodiment, a subset of compounds of Formula (III) includes those of Formula (IIIa):

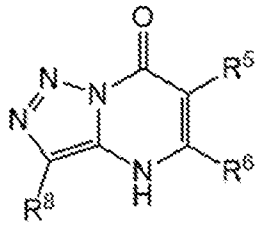


(IIIa),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, wherein Y_1 is -O-, -NH-, -NR^{24}-, or -S-, and Y_2, Y_3, Y_4, and Y_5 are -N= or -CR^{25}=, provided that 0, 1 or 2 of Y_2, Y_3, Y_4, and Y_5 are -N=; wherein R^{24} is selected from the group consisting of C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; and phenyl optionally substituted with one halo, -CN, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl or -N(C_{1-3}alkyl)$_2$; and wherein R^{25} is H or R^{17}, wherein R^{17} is as defined for compounds of Formula (III), provided that 0, 1, 2 or 3 of Y_2, Y_3, Y_4, and Y_5 are -CR^{25}= wherein R^{25} is R^{17}; and wherein R^6, R^7 and R^8 are as defined for compounds of Formula (III).

[0077] In one embodiment of compounds of Formula (IIIa), R^6 is -CN or C_{1-3}alkyl optionally substituted with one -NH_2, -NHC_{1-3}alkyl, -N(C_{1-3}alkyl)$_2$, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -S(=O)$_m$$C_{1-3}$alkyl, -C(=O)$C_{1-3}$alkyl, -$OR^{23}$, or 5- or 6-membered monocyclic heteroaryl, wherein monocyclic heteroaryl is optionally substituted with 1 or 2 C_{1-3}alkyl; and R^7 is -CN or -CF_3, wherein R^{23} is as defined for compounds of Formula (III).

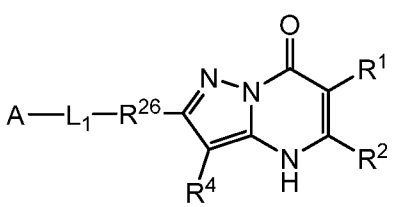
[0078] In another aspect, the present invention provides the compounds of Formula (IV):



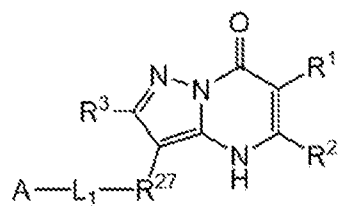
(IV),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In this formula R^5, R^6, and R^8 are as defined for compounds of Formula (III), and provided the compound is not wherein R^5 is unsubstituted phenyl, R^6 is H and R^8 is 2-fluoro-phenyl.

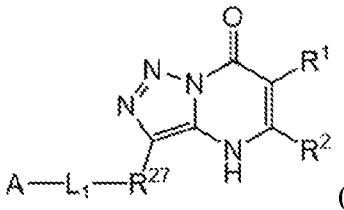
[0079] In another aspect, conjugates are provided comprising compounds of the invention linked to a suitable ligand. In one embodiment, compounds of Formula I can be modified by replacing or modifying the R^3 or R^4 substituent, e.g. in compounds of Formula IA, or by replacing or modifying the R^4 substituent in compounds of Formula IA', to provide a suitable substituent comprising a reactive group capable of binding to a suitable linker. In some embodiments, the reactive group comprises a suitable hydroxy or amine group (e.g. an R^3 or R^4 substituent or modification thereof comprising a terminal -OH, $-NH_2$, $C(=O)NH_2$, and the like) that is capable of reacting with a suitable linker. In one embodiment, compounds of Formula I can be modified by replacing or modifying the R^3 or R^4 substituent, e.g. in compounds of Formula IA, or by replacing or modifying the R^4 substituent in compounds of Formula IA', to provide a suitable substituent bound to a linker moiety, wherein said linker moiety comprises a reactive group capable of binding to a suitable ligand. In one embodiment, compounds of Formula I can be modified by replacing or modifying the R^3 or R^4 substituent, e.g. in compounds of Formula IA, or by replacing or modifying the R^4 substituent in compounds of Formula IA', to provide a suitable substituent bound to a linker moiety, wherein said linker moiety is bound to a suitable ligand. In one embodiment, the ligand binds to an E3 ubiquitin ligase. In some embodiments, the E3 ubiquitin ligase is MDM2, cIAP1, CRBN, or VHL. In one embodiment, a modified compound of the invention is a compound of Formula (Va), Formula (Vb), or Formula (Vc):



(Va),



(Vb), or



(Vc),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In these formulae, A is an E3 ubiquitin ligase ligand; L_1 is a suitable linker, R^{26} is a suitable R^3 or modification or replacement of R^3 (as defined in Formula I), and R^{27} is a suitable R^4 or modification or replacement of R^4 (as defined in Formula I); and R^1, R^2, R^3, and R^4 are as defined for compounds of Formula (I).

[0080] Representative compounds of the present invention include compounds listed in Table 1 (by name in Table 1A and structure in Table 1B).

[0081] In reference to the present invention comprising a compound as disclosed herein, the compound includes a compound of Formula I (including IA, IA', Ia, Ia', Ib and Ib'), Formula II (i.e. including IIa, IIa', IIb, IIb', IIc, IIc', IId, IId', IIe, IIe', IIf and IIf'), Formula III (including IIIa) or Formula IV and all embodiments thereof, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof.

[0082] The present invention provides a pharmaceutical composition comprising a compound as disclosed herein, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof together with a pharmaceutically acceptable diluent or carrier.

[0083] The present provides a kit comprising a compound as disclosed herein, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, including any container, pack, or dispenser together with instructions for administration.

[0084] The present invention provides a compound as disclosed herein, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, for use in the treatment of a cGAS/STING pathway-mediated condition.

[0085] The present invention provides a method of inhibiting the cGAS/STING pathway in a cell, comprising contacting the cell with one or more compounds or compositions of the present invention.

[0086] The present invention provides a method of inhibiting cytokine production in a cell, comprising contacting the cell with one or more compounds or compositions of the present invention, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof.

[0087] The present invention provides a method of treating a cGAS/STING pathway-mediated condition, comprising administering to a subject in need thereof an effective amount of one or more compounds or compositions of the present invention, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof.

[0088] For example, the cGAS/STING pathway-mediated condition is an autoimmune, inflammatory, or neurodegenerative condition. For example, wherein the disease is selected from the group consisting of systemic inflammatory response syndrome (SIRS), sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature) syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis, vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease.

[0089] For example, wherein the disease is SIRS, sepsis, septic shock, atherosclerosis, celiac disease, interstitial cystitis, transplant rejection, Aicardi-Goutieres Syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, spondyloenchondrodysplasia, psoriasis, Type 1 diabetes, Type 2 diabetes, or Sjogren's syndrome.

[0090] A method of treating an inflammatory disease in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of one or more compounds or

compositions of the present invention, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof.

[0091] For example, wherein the disease is rheumatoid arthritis, juvenile rheumatoid arthritis, inflammatory bowel disease (ulcerative colitis, Crohn's disease), age-related macular degeneration, IgA nephropathy, glomerulonephritis, vasculitis, polymyositis, or Wegener's disease.

[0092] Another aspect of the invention provides a method of treating neurodegenerative diseases in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of one or more compounds or compositions of the present invention, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof.

[0093] For example, wherein the disease is Alzheimer's disease, Parkinson's disease, multiple sclerosis, IgM polyneuropathies, or myasthenia gravis.

[0094] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents and other references mentioned herein are incorporated by reference. The references cited herein are not admitted to be prior art to the claimed invention. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods and examples are illustrative only and are not intended to be limiting.

[0095] Other features and advantages of the invention will be apparent from the following detailed description and claims.

DRAWINGS

[0096] Fig. 1 depicts the expression of cytokines RANTES or MCP-1 along with cell viability as a function of the Log_{10} concentration (μM) of compound C1089 in Trex1-KO mice bone marrow-derived macrophages.

DETAILED DESCRIPTION

[0097] STING (STimulator of INterferon Genes) is a central mediator for a cytosolic pathway that triggers type I interferon, in response to sensing cytosolic double-stranded (ds)

DNA from infectious pathogens or aberrant host cells (Danger Associated Molecular Patterns, DAMPS) (Barber, Immunol. Rev 243: 99-108, 2011). Alternatively known as TMEM173, MITA, ERIS, and MPYS, STING was discovered using cDNA expression cloning methods as a MyD88-independent host cell defense factor expressed in macrophages, dendritic cells (DCs) and fibroblasts was found to induce expression of IFN-β and NF-κB dependent pro-inflammatory cytokines in response to sensing cytoplasmic DNA, in response to infection with herpes simplex virus (Ishikawa and Barber, Nature 455: 674-79, 2008).

[0098] While STING was discovered as being the critical sensor for inducing the production of IFN-β in response to infection with herpes simplex virus, the mechanism for this sensing function initially remained elusive. This conundrum was solved with the discovery of cyclic GMP-AMP synthase (cGAS), a host cell nucleotidyl transferase that directly binds dsDNA, and in response synthesizes a second messenger, c[G(2',5')pA(3',5')p] (cyclic GMP-AMP or 2'3'-cGAMP), which activates the STING pathway and induces IFN-β expression (Sun et al., Science 339: 786-91, 2013; Wu et al., Science 339: 826-30, 2013). This 2'3'-cGAMP product differed from bacterial-derived canonical cyclic dinucleotides, which were shown to respond differently to single nucleotide polymorphisms in the hSTING gene (Diner et al., Cell Reports 3:1355-1361, 2013; Gao et al., Cell 154:748-762, 2013; Conlon et. al., J Immunol 190:5216-5225, 2013). It was demonstrated that, while the bacterial-derived cyclic dinucleotides contained bis-3'-5' linkages, cGAS produces a non-canonical, *i.e.*, mixed linkage, CDN represented as c[G(2',5')pA(3',5')p] (Diner et al., Cell Reports 3:1355-1361, 2013; Gao et al., Cell 153:1094-1107, 2013; Ablasser et al., Nature 498: 380–84, 2013; Kranzusch et al., Cell Reports 3: 1362-68, 2013; Zhang et al., Mol. Cell. 51: 226-35, 2013). Cells without a functional cGAS are unable to express IFN-β in response to stimulation with cytosolic DNA.

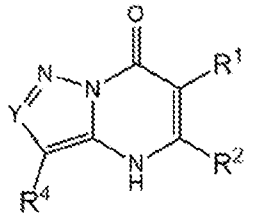
[0099] Given the role of cGAS in the STING pathway and the role of type I interferons in various diseases, treatment with a cGAS/STING pathway inhibitor may have therapeutic benefit in a number of inflammatory, autoimmune, and neurodegenerative diseases, including, but are not limited to, systemic inflammatory response syndrome (SIRS), sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature) syndrome, chilblain lupus erythematosus, systemic lupus erythematosus,

rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis, vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease. See, for example, Krienkamp et al., Cell Reports 22:2006–2015, 2018; Kerur et al., *Nature Medicine* 24:50–61, 2018; Yang et al., PNAS 114 (23): E4612-E4620, 2017; King et al., *Nature Medicine* 23:1481–1487, 2017; Bai et al., PNAS 114 (46):12196-12201, 2017; Ahn et al., Cell Reports 21:3873–3884, 2017; Li et al., J. Experimental Medicine, 215(5) 1287, 2018. In some embodiments, compounds of the invention are useful in treating Aicardi-Goutieres Syndrome, X-linked reticulate pigmentary disorder, dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, or Type I or Type II diabetes.

[00100] The present invention provides novel pyrazolopyrimidinone or triazolopyrimidinone compounds, synthetic methods for making the compounds, pharmaceutical compositions containing them and various uses of the compounds.

Pyrazolopyrimidinone and Triazolopyrimidinone compounds

[00101] The present invention provides the compounds of Formula (I), including Formula (IA) and Formula (IA'):



(I),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In this formula:

Y is $-CR^3=$ or $-N=$;

R^1 is Q^1-T^1-$(X^1)_n$;

Q^1 is a bond or C_{1-3}alkylene, wherein the C_{1-3}alkylene group is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w2}$, and $-NR^{w2}R^{x2}$;

T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-

membered heteroaryl, -C(=O)C_{0-3}alkylene-C_{3-8}cycloalkyl, -C(=O)-C_{0-3}alkylene-C_{6-10}aryl, -C(=O)-C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, -C(=O)-C_{0-3}alkylene-5 to 10-membered heteroaryl, -NR^aR^b, -$S(=O)_2R^a$, -$NR^aC(=O)R^a$, -$NR^aC(=O)NR^aR^b$, -$NR^aC(=O)OR^a$, -$NR^aS(=O)_2R^a$, -$C(=O)NR^aS(=O)_2R^a$, -$NR^aS(=O)_2NR^aR^b$, -$C(=O)NR^aR^b$, or -$S(=O)_2NR^aR^b$;

each X^1 is independently selected from the group consisting of halo, cyano, oxo, C_{0-3}alkylene-$C(=O)R^c$, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-$C(=O)OR^c$, C_{0-3}alkylene-$OC(=O)R^c$, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$N^+R^cR^dR^{d'}$, C_{0-3}alkylene-$S(=O)_mR^c$, C_{0-3}alkylene-$NR^cC(=O)R^c$, C_{0-3}alkylene-$NR^cC(=O)NR^cR^d$, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=O)OR^c$, C_{0-3}alkylene-$NR^cS(=O)_2R^c$, C_{0-3}alkylene-$C(=O)NR^cS(=O)_2R^c$, C_{0-3}alkylene-$NR^cS(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=O)NR^cR^d$, C_{0-3}alkylene-$S(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, and R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S1} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, nitro, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$NR^eC(=O)R^e$, C_{0-3}alkylene-$NR^eC(=O)OR^e$, C_{0-3}alkylene-$NR^eC(=O)NR^eR^f$, C_{0-3}alkylene-$OC(=O)R^e$, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-3}alkylene-$C(=O)NR^eR^f$, C_{0-3}alkylene-$C(=O)R^e$, C_{0-3}alkylene-$S(=O)_mR^e$, C_{0-3}alkylene-$S(=O)_2NR^eR^f$, C_{0-3}alkylene-$NR^eS(=O)_2R^e$, C_{0-3}alkylene-$C(=O)NR^eS(=O)_2R^e$, C_{0-3}alkylene-$NR^eS(=O)_2NR^eR^f$, and R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl,

and each R^{S2} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^w, and -NR^wR^x;

R^2 is Q^2-T^2-$(X^2)_p$;

Q^2 is a bond or C_{1-3}alkylene, wherein the C_{1-3}alkylene group is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w3}, and -$NR^{w3}R^{x3}$;

T^2 is H, halo, cyano, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl,

C(=O)-C_{0-3}alkylene-C_{3-8}cycloalkyl, C(=O)-C_{0-3}alkylene-C_{6-10}aryl, C(=O)-C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C(=O)-C_{0-3}alkylene-5- to 10-membered heteroaryl, $-OR^z$, $-S(=O)_mR^k$, $-P(=O)R^{kk}R^{mm}$, $-NR^kR^m$, $-C(=O)OR^k$, or $-C(=O)NR^kR^m$;

each X^2 is independently selected from the group consisting of halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-$C(=O)OR^n$, and R^{S3}, in which R^{S3} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and R^{S3} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^p, C_{0-3}alkylene-$S(=O)_mR^p$, C_{0-3}alkylene-NR^pR^q, C_{0-3}alkylene-$C(=O)NR^pR^q$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^p$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S4}, in which R^{S4} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S4} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w4}$, and $-NR^{w4}R^{x4}$;

R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, -CN, $-OR^r$, $-C(=O)R^r$, $-S(=O)_mR^r$, NR^rR^t, or $-C(=O)OR^r$, wherein C_{1-3}alkyl, C_{2-3}alkenyl and C_{2-3}alkynyl are optionally substituted with one C_{3-6}cycloalkyl;

R^4 is C_{1-6}alkyl, C_{1-6}haloalkyl, $S(=O)_mR^u$, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl, wherein C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, OR^{w5}, and $NR^{w5}R^{x5}$;

each of R^a and R^b, independently, is H or R^{S5}, in which R^{S5} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and R^{S5} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, C_{0-3}alkylene-$OC(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)NR^{c2}R^{d2}$, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-$S(=O)_2NR^{c2}R^{d2}$,

C_{0-3}alkylene-$NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$C(=O)NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2NR^{c2}R^{d2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S6} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{e2}R^{f2}$, C_{0-3}alkylene-OR^{e2}, C_{0-3}alkylene-$NR^{e2}C(=O)R^{e2}$, C_{0-3}alkylene-$NR^{e2}C(=O)OR^{e2}$, C_{0-3}alkylene-$NR^{e2}C(=O)NR^{e2}R^{f2}$, C_{0-3}alkylene-$OC(=O)R^{e2}$, C_{0-3}alkylene-$C(=O)OR^{e2}$, C_{0-3}alkylene-$C(=O)NR^{e2}R^{f2}$, C_{0-3}alkylene-$C(=O)R^{e2}$, C_{0-3}alkylene-$S(=O)_mR^{e2}$, C_{0-3}alkylene-$S(=O)_2NR^{e2}R^{f2}$, C_{0-3}alkylene-$NR^{e2}S(=O)_2R^{e2}$, C_{0-3}alkylene-$C(=O)NR^{e2}S(=O)_2R^{e2}$, C_{0-3}alkylene-$NR^{e2}S(=O)_2NR^{e2}R^{f2}$, and R^{S7}, in which R^{S7} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S7} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w6}$, and $-NR^{w6}R^{x6}$;

each of R^c, R^{c2}, R^d, $R^{d'}$, and R^{d2}, independently, is H or R^{S8}, in which R^{S8} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S8} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{e3}R^{f3}$, C_{0-3}alkylene-OR^{e3}, C_{0-3}alkylene-$C(=O)OR^{e3}$, C_{0-3}alkylene-$C(=O)NR^{e3}R^{f3}$, C_{0-3}alkylene-$C(=O)R^{e3}$, C_{0-3}alkylene-$S(=O)_mR^{e3}$, C_{0-3}alkylene-$S(=O)_2NR^{e3}R^{f3}$, C_{0-3}alkylene-$NR^{f3}C(=O)R^{e3}$, C_{0-3}alkylene-$NR^{f3}S(=O)_mR^{e3}$, and R^{S9}, in which R^{S9} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S9} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w7}$, and $-NR^{w7}R^{x7}$;

each of R^e, R^{e2}, R^{e3}, R^f, R^{f2}, and R^{f3}, independently, is H or R^{S10}, in which R^{S10} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered

heteroaryl;

and each R^{S10} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w8}, and -$NR^{w8}R^{x8}$;

each of R^{kk}, and R^{mm}, is independently selected from the group consisting of R^k, -OR^k, and -NR^kR^m;

each of R^k, and R^m, independently, is H or R^z, in which R^z is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^z is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{n2}R^{o2}$, C_{0-3}alkylene-OR^{n2}, C_{0-3}alkylene-$C(=O)OR^{n2}$, C_{0-3}alkylene-$C(=O)NR^{n2}R^{o2}$, C_{0-3}alkylene-$C(=O)R^{n2}$, C_{0-3}alkylene-$S(=O)_mR^{n2}$, C_{0-3}alkylene-$S(=O)_2NR^{n2}R^{o2}$, and R^{S11}, in which R^{S11} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S11} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p2}, C_{0-3}alkylene-$S(=O)_mR^{p2}$, C_{0-3}alkylene-$NR^{p2}R^{q2}$, C_{0-3}alkylene-$C(=O)NR^{p2}R^{q2}$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^{p2}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S12}, in which R^{S12} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S12} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w9}, and -$NR^{w9}R^{x9}$;

each of R^n, R^{n2}, R^o, and R^{o2}, independently, is H or R^{S13}, in which R^{S13} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S13} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p3}, C_{0-3}alkylene-$S(=O)_mR^{p3}$, C_{0-3}alkylene-$NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)OR^{p3}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S14}, in which R^{S14} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S14} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w10}, and -$NR^{w10}R^{x10}$;

each of R^p, R^{p2}, R^{p3}, R^q, R^{q2}, and R^{q3}, independently, is H or R^{S15}, in which R^{S15} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S15} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w11}, and -$NR^{w11}R^{x11}$;

each of R^r, R^t, and R^u, independently, is H or R^{S16}, in which R^{S16} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S16} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -$C(=O)OR^{w12}$, -OR^{w12}, and -$NR^{w12}R^{x12}$;

each R^w, R^{w2}, R^{w3}, R^{w4}, R^{w5}, R^{w6}, R^{w7}, R^{w8}, R^{w9}, R^{w10}, R^{w11}, R^{w12}, R^x, R^{x2}, R^{x3}, R^{x4}, R^{x5}, R^{x6}, R^{x7}, R^{x8}, R^{x9}, R^{x10}, R^{x11}, and R^{x12}, independently, is H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl;

each of n and p independently is 0, 1, 2, 3, 4, or 5, wherein when T^2 is H, p is 0; and

m is 0, 1, or 2;

with the proviso that, for compounds where Y is -CR^3=:

a) when R^1 is unsubstituted phenyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl, unsubstituted phenyl, or unsubstituted pyridine;

b) when R^1 is unsubstituted cyclohexyl, R^2 is methyl and R^3 is methyl, R^4 is not unsubstituted pyridine;

c) when R^1 is unsubstituted cyclopentyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl or unsubstituted pyridine,

d) when R^2 is methyl, R^3 is methyl and R^4 is 3,4-di-ethoxy-phenyl, R^1 is not unsubstituted 1-pyrrolidine, unsubstituted 1-piperidine, 4-methyl-1-piperidine, 4-(phenylmethyl)-1-piperidine, unsubstituted 2-1,2,3,4-tetrahydro-isoquinoline, unsubstituted morpholine, or $NHCH_2CH_2$-3-indole;

e) when R^1 is unsubstituted CH_2-phenyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl, trifluoromethyl, 1-methyl-piperidin-4-yl, unsubstituted pyridine, unsubstituted phenyl,

phenyl mono-substituted with 4-F, 4-Cl, 2-methoxy or 4-methoxy, or phenyl disubstituted with 3,4-methoxy;

f) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted pyridine, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 4-CN, 4-NO_2, 4-F or 2-F;

g) when R^2 is methyl, R^3 is methyl and R^4 is ethyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 4-CN or 4-NO_2;

h) when R^2 is methyl, R^3 is methyl and R^4 is 4-methoxy-phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 3-Cl, 4-Br, 2-methyl or 4-methyl;

i) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 3-Cl, 4-Cl, 4-Br, 2-methyl, 3-methyl, 4-methyl, 4-isopropyl or 4-*tert*-butyl; or R^1 is not unsubstituted CH_2-1-naphthylene or unsubstituted CH_2-pyridine;

j) when R^2 is methyl, R^3 is methyl and R^4 is 4-Cl-phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 4-Cl or 4-isopropyl;

k) when R^1 is unsubstituted CH_2-phenyl, R^2 is methyl and R^3 is trifluoromethyl, R^4 is not unsubstituted phenyl or phenyl substituted with 2-Cl or 4-Cl;

l) the compound is not wherein R^1 is CH_2-4-Br-phenyl, R^2 is methyl, R^3 is ethyl and R^4 is unsubstituted phenyl;

m) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not $CH_2CH_2C(=O)NH$-phenyl wherein the phenyl ring is unsubstituted or is substituted at the 4-position with Cl, methyl or methoxy;

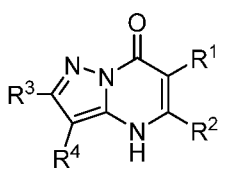
n) when R^2 is methyl or ethyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not substituted pyrazolo[1,5-*a*]pyrimidin-7-yl;

o) when R^2 is H, R^3 is isopropyl and R^4 is methyl, R^1 is not unsubstituted pyrazole; and

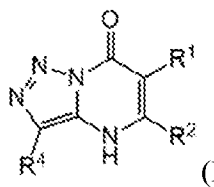
p) the compound is not wherein R^1 is unsubstituted CH_2-phenyl, R^2 is H, R^3 is methyl and R^4 is unsubstituted phenyl; and

with the proviso that, for compounds where Y is -N=, the compound is not wherein R^1 is unsubstituted phenyl, R^2 is H and R^4 is 2-fluoro-phenyl.

[00102] For example, the compound can be of Formula (IA) or Formula (IA'):



(IA) or



(IA').

[00103] For example, Q^1 is a bond or $-CH_2-$ and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, or $-C(=O)NR^aR^b$.

[00104] For example, Q^1 is a bond and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[00105] For example, Q^1 is a bond and T^1 is C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[00106] For example Q^1 is a bond and T^1 is phenyl, 5- or 6-membered monocyclic heteroaryl, or 9- or 10-membered bicyclic heteroaryl, preferabley wherein T^1 is 9- or 10-membered bicyclic heteroaryl.

[00107] For example, Q^1 is a bond or $-CH_2-$, T^1 is $-C(=O)NR^aR^b$ and n is 0.

[00108] For example, one of R^a and R^b is H or methyl and the other of R^a and R^b is not H or methyl.

[00109] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^n$, and each R^n and R^o is independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl.

[00110] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or $-OC_{1-6}$alkyl.

[00111] For example, R^2 is H, cyano, methyl or methoxymethyl.

[00112] For example, R^2 is H, methyl or methoxymethyl.

[00113] For example, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, -CN, $-S(=O)_2C_{1-3}$alkyl or $-C(=O)OC_{1-3}$alkyl.

[00114] For example, R^3 is -CN, C_{1-3}alkyl, C_{1-3}haloalkyl or $-C(=O)OC_{1-3}$alkyl.

[00115] For example, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl or $-C(=O)OC_{1-3}$alkyl.

[00116] For example, R^3 is $-CF_3$, methyl or $-C(=O)OC_{1-3}$alkyl.

[00117] For example, R^3 is $-CF_3$ or -CN.

[00118] For example, R^3 is $-CF_3$

[00119] For example, R^3 is -CN.

[00120] For example, R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, -S(=O)$_2C_{1-3}$alkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$.

[00121] For example, R^4 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein Rw5 and Rx5 are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00122] For example, R^4 is C_{3-8}cycloalkyl or C_{6-10}aryl, wherein C_{3-8}cycloalkyl and C_{6-10}aryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00123] For example, R^4 is phenyl optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

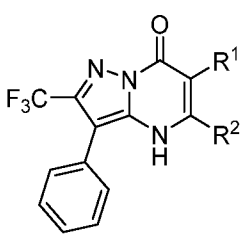
[00124] For example, R^4 is C_{3-8}cycloalkyl.

[00125] For example, R^4 is cyclopentyl.

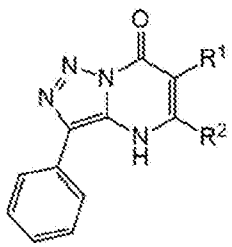
[00126] For example, R^4 is C_{6-10}aryl.

[00127] For example, R^4 is phenyl.

[00128] For example, the compound can be of Formula (Ia) or Formula (Ia'):



(Ia) or



(Ia').

[00129] For example, Q^1 is a bond or -CH_2-.

[00130] For example, T^1 is -C(=O)-C_{0-1}alkylene-C_{6-10}aryl or -C(=O)-C_{0-1}alkylene-5 to 10-membered heteroaryl.

[00131] For example, Q^1 is a bond or -CH_2- and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, or -C(=O)NR^aR^b .

[00132] For example, Q^1 is a bond and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[00133] For example, Q^1 is a bond and T^1 is C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[00134] For example Q^1 is a bond and T^1 is phenyl, 5- or 6-membered monocyclic heteroaryl, or 9- or 10-membered bicyclic heteroaryl, preferabley wherein T^1 is 9- or 10-membered bicyclic heteroaryl.

[00135] For example, T^1 is C(=O)NR^aR^b and n is 0.

[00136] For example, one of R^a and R^b is H or methyl and the other of R^a and R^b is not H or methyl.

[00137] For example, n is 0.

[00138] For example, T^1 is aryl or heteroaryl, preferably phenyl, 5- or 6-membered monocyclic heteroaryl, or 9- or 10-membered bicyclic heteroaryl.

[00139] For example, T^1 is 5- to 10-membered heteroaryl.

[00140] For example, T^1 is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indolinyl, isoindolyl, isoindolinyl, indazolyl, pyrazolopyridinyl, pyrazolopyrimidinyl, oxazolopyrimidinyl, oxazolopyridinyl, imidazopyridinyl, benzimidazolyl, tetrahydrobenzimidazolyl, benzofuranyl, dihydrobenzofuranyl, isobenzofuranyl, dihydroisobenzofuranyl, triazolopyridinyl, benzothiazolyl, azabenzimidazolyl, azabenzoxazolyl, azabenzothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, benzodioxolyl, chromanyl, tetrahydrooxazoloazepinyl, tetrahydrobenzoxazolyl, oxadiazolyl, thiadiazolyl, pyrazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl.

[00141] For example, T^1 is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, pyrazolopyridinyl, benzimidazolyl, benzothiazolyl, azabenzimidazolyl, azabenzoxazolyl, azabenzothiazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, tetrahydrobenzoxazolyl, tetrahydrobenzimidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl.

[00142] For example, T^1 is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, pyrazolopyridinyl, benzimidazolyl, benzothiazolyl, azabenzimidazolyl, azabenzoxazolyl, azabenzothiazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, tetrahydrobenzoxazolyl, tetrahydrobenzimidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl, and X^1 is halo, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-NR^cR^d, or R^{S1}, in which R^{S1} is C_{1-6}alkyl or C_{0-3}alkylene-C_{3-8}cycloalkyl.

[00143] For example, T^1 is C_{0-1}alkylene-C_{6-10}aryl.

[00144] For example, T^1 is phenyl, benzyl, naphthyl, or CH_2naphthyl.

[00145] For example, T^1 is 3- to 12-membered heterocycloalkyl, preferably 4- to 10--membered heterocycloalkyl.

[00146] For example, T^1 is piperazine, piperidine, quinuclidine, or morpholine.

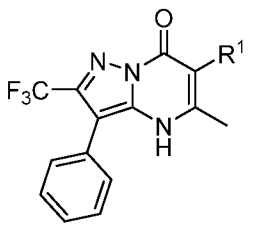
[00147] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5 to 10-membered heteroaryl, each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^n$, and each R^n and R^o is independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl.

[00148] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or OC_{1-6}alkyl.

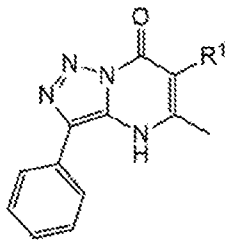
[00149] For example, R^2 is H, cyano, methyl or methoxymethyl.

[00150] For example, R^2 is H, methyl or methoxymethyl.

[00151] The present invention provides the compounds of Formula (Ib) or Formula (Ib'):



(Ib) or



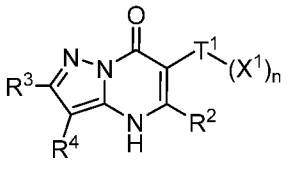
(Ib').

[00152] In some embodiments of Formula Ib or Ib', Q^1 is a bond or -CH_2- and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, or -$C(=O)NR^aR^b$.

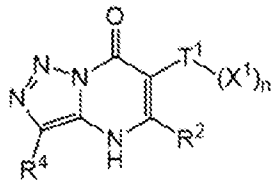
[00153] In some embodiments of Formula Ib or Ib', Q^1 is a bond and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl.

[00154] In some embodiments of Formula Ib or Ib', Q^1 is a bond or -CH_2- and T^1 is -C(=O)NR^aR^b and n is 0.

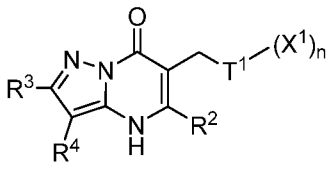
[00155] Another subset of the compounds of Formula (I) includes those of Formula (IIa), Formula (IIa'), Formula (IIb) or Formula (IIb'):



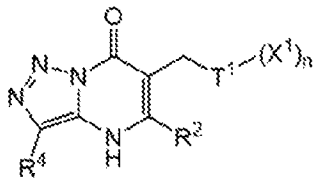
(IIa),



(IIa'),



(IIb), or



(IIb'),

R^2, R^3, R^4, T^1, X^1 and n are as defined for Formula I.

[00156] In some embodiments of Formula IIa, IIa', IIb, or IIb', T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, or C(=O)NR^aR^b.

[00157] In some embodiments of Formula IIa, or IIa', T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5 to 10-membered heteroaryl.

[00158] In some embodiments of Formula IIa, IIa', IIb, or IIb', T^1 is -C(=O)NR^aR^b and n is 0.

[00159] In some embodiments of Formula IIa, IIa', IIb or IIb', R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-C(=O)NR^nR^o, C_{0-3}alkylene-C_{0-3}alkylene-C(=O)OR^n, and each R^n and R^o is independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl.

[00160] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or -OC_{1-6}alkyl.

[00161] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^2 is H, cyano, methyl or methoxymethyl.

[00162] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^2 is H, methyl or methoxymethyl.

[00163] In some embodiments of Formula IIa or IIb, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, -CN, -$S(=O)_2C_{1-3}$alkyl or -C(=O)OC_{1-3}alkyl.

[00164] In some embodiments of Formula IIa or IIb, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl or -C(=O)OC_{1-3}alkyl.

[00165] In some embodiments of Formula IIa or IIb, R^3 is -CN, $-CF_3$, methyl or -C(=O)OC_{1-3}alkyl.

[00166] In some embodiments of Formula IIa or IIb, R^3 is -CN or $-CF_3$.

[00167] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, -S(=O)$_2$$C_{1-3}$alkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$.

[00168] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^4 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$, wherein Rw5 and Rx5 are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00169] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^4 is C_{3-8}cycloalkyl or C_{6-10}aryl, wherein C_{3-8}cycloalkyl and C_{6-10}aryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00170] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^4 is C_{3-8}cycloalkyl.

[00171] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^4 is cyclopentyl.

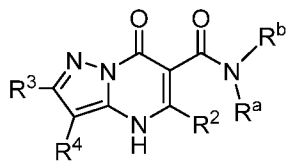
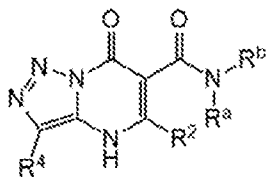
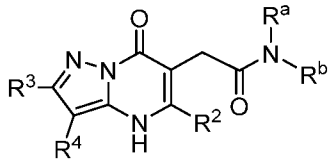
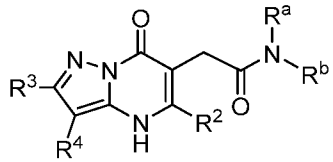
[00172] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^4 is C_{6-10}aryl.

[00173] In some embodiments of Formula IIa, IIa', IIb, or IIb', R^4 is phenyl.

[00174] In some embodiments of Formula IIa, IIa', IIb, or IIb', T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, -C(=O)-C_{0-3}alkylene-C_{3-8}cycloalkyl, -C(=O)-C_{0-3}alkylene-C_{6-10}aryl, -C(=O)-C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, -C(=O)-C_{0-3}alkylene-5- to 10-membered heteroaryl, $-NR^aR^b$, $-S(=O)_2R^a$, $-NR^aC(=O)R^a$, $-NR^aC(=O)NR^aR^b$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^a$, $-C(=O)NR^aS(=O)_2R^a$, $-NR^aS(=O)_2NR^aR^b$, $-C(=O)NR^aR^b$, or $-S(=O)_2NR^aR^b$; each X^1 independently is halo, cyano, oxo, C_{0-3}alkylene-$C(=O)R^c$, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-

$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, or R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5 to 10-membered heteroaryl, and R^{S1} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$NR^eC(=O)R^e$, C_{0-3}alkylene-$NR^eC(=O)OR^e$, C_{0-3}alkylene-$NR^eC(=O)NR^eR^f$, C_{0-3}alkylene-$OC(=O)R^e$, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-3}alkylene-$C(=O)R^e$, C_{0-3}alkylene-$S(=O)_mR^e$, C_{0-3}alkylene-$S(=O)_2NR^eR^f$, C_{0-3}alkylene-$NR^eS(=O)_2R^e$, C_{0-3}alkylene-$NR^eS(=O)_2NR^eR^f$, and R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl, and R^{S2} is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^w$, and $-NR^wR^x$.

[00175] Yet another subset of the compounds of Formula I includes those of Formula (IIc), Formula (IIc'), Formula (IId), or Formula (IId'):


(IIc),

(IIc'),

(IId), or

(IId'),

R^2, R^3, R^4, R^a and R^b are as defined for Formula I.

[00176] In some embodiments of Formula IIc, IIc', IId, or IId', R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5 to 10-membered heteroaryl, each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^n$, and each R^n and R^o is independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl.

[00177] In some embodiments of Formula IIc, IIc', IId, or IId', R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or OC_{1-6}alkyl.

[00178] In some embodiments of Formula IIc, IIc', IId, or IId', R^2 is H, cyano, methyl or methoxymethyl.

[00179] In some embodiments of Formula IIc, IIc', IId, or IId', R^2 is H, methyl or methoxymethyl.

[00180] In some embodiments of Formula IIc or IId, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, -CN, -S(=O)$_2C_{1-3}$alkyl or -C(=O)OC_{1-3}alkyl

[00181] In some embodiments of Formula IIc or IId, R^3 is -CN, C_{1-3}alkyl, C_{1-3}haloalkyl or -C(=O)OC_{1-3}alkyl.

[00182] In some embodiments of Formula IIc or IId, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl or -C(=O)OC_{1-3}alkyl.

[00183] In some embodiments of Formula IIc or IId, R^3 is -CN, $-CF_3$, methyl or -C(=O)OC_{1-3}alkyl.

[00184] In some embodiments of Formula IIc or IId, R^3 is -CN or $-CF_3$.

[00185] In some embodiments of Formula IIc, IIc', IId, or IId', R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, -S(=O)$_2C_{1-3}$alkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$.

[00186] In some embodiments of Formula IIc, IIc', IId, or IId', R^4 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5 to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein Rw5 and Rx5 are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00187] In some embodiments of Formula IIc, IIc', IId, or IId', R^4 is C_{3-8}cycloalkyl or C_{6-10}aryl, wherein C_{3-8}cycloalkyl and C_{6-10}aryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

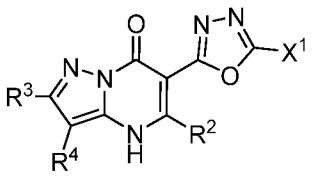
[00188] In some embodiments of Formula IIc, IIc', IId, or IId', R^4 is C_{3-8}cycloalkyl.

[00189] In some embodiments of Formula IIc, IIc', IId, or IId', R^4 is cyclopentyl.

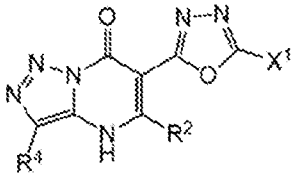
[00190] In some embodiments of Formula IIc or IId IIc, IIc', IId, or IId', R^4 is C_{6-10}aryl.

[00191] In some embodiments of Formula IIc, IIc', IId, or IId', R^4 is phenyl.

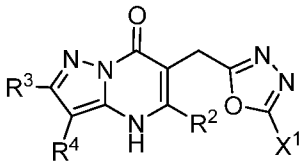
[00192] Still another subset of the compounds of Formula (I) includes those of Formula (IIe), Formula (IIe'), Formula (IIf), or Formula (IIf'):



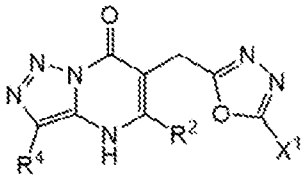
(IIe), or



(IIe'),



(IIf), or



(IIf')

wherein each X^1 independently is halo, cyano, C_{0-3}alkylene-C(=O)R^c, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-C(=O)OR^c, C_{0-3}alkylene-OC(=O)R^c, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$S(=O)_mR^c$, C_{0-3}alkylene-$NR^cC(=O)R^c$, C_{0-3}alkylene-$NR^cC(=O)NR^cR^d$, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=O)OR^c$, C_{0-3}alkylene-$NR^cS(=O)_2R^c$, C_{0-3}alkylene-$C(=O)NR^cS(=O)_2R^c$, C_{0-3}alkylene-$NR^cS(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=O)NR^cR^d$, C_{0-3}alkylene-$S(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, or R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl, R^2, R^3, R^4, R^c, R^d and R^{S1} are as defined for Formula I.

[00193] In some embodiments of Formula IIe, IIe', IIf or IIf', R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5 to 10-membered heteroaryl, each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^n$, and each R^n and R^o is independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl.

[00194] In some embodiments of Formula IIe, IIe', IIf or IIf', R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or -OC_{1-6}alkyl.

[00195] In some embodiments of Formula IIe, IIe', IIf or IIf', R^2 is H, cyano, methyl or methoxymethyl.

[00196] In some embodiments of Formula IIe, IIe', IIf or IIf', R^2 is H, methyl or methoxymethyl.

[00197] In some embodiments of Formula IIe or IIf, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, -CN, $S(=O)_2C_{1-3}$alkyl or -$C(=O)OC_{1-3}$alkyl

[00198] In some embodiments of Formula IIe or IIf, R^3 is -CN, C_{1-3}alkyl, C_{1-3}haloalkyl or -C(=O)OC_{1-3}alkyl.

[00199] In some embodiments of Formula IIe or IIf, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl or -C(=O)OC_{1-3}alkyl.

[00200] In some embodiments of Formula IIe or IIf, R^3 is -CN, $-CF_3$, methyl or -C(=O)OC_{1-3}alkyl.

[00201] In some embodiments of Formula IIe or IIf, R^3 is -CN or $-CF_3$.

[00202] In some embodiments of Formula IIe, IIe', IIf or IIf', R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, S(=O)$_2C_{1-3}$alkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$.

[00203] In some embodiments of Formula IIe, IIe', IIf or IIf', R^4 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5 to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5 to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$, wherein Rw5 and Rx5 are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00204] In some embodiments of Formula IIe, IIe', IIf or IIf', R^4 is C_{3-8}cycloalkyl or C_{6-10}aryl, wherein C_{3-8}cycloalkyl and C_{6-10}aryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, OR^{w5}, and $NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00205] In some embodiments of Formula IIe, IIe', IIf or IIf', R^4 is C_{3-8}cycloalkyl.

[00206] In some embodiments of Formula IIe, IIe', IIf or IIf', R^4 is cyclopentyl.

[00207] In some embodiments of Formula IIe, IIe', IIf or IIf', R^4 is C_{6-10}aryl.

[00208] In some embodiments of Formula IIe, IIe', IIf or IIf', R^4 is phenyl.

[00209] Any of the substituents described herein for any of R^1, R^2, R^3, R^4, R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^i, R^j, R^k, R^m, R^n, R^p, R^r, R^t, R^u, R^w, R^{w2}, R^x, R^z, R^{x2}, R^{S1}, R^{S2}, R^{S3}, R^{S4}, Q^1, Q^2, T^1, T^2, X^1, and X^2 can be combined with any of the substituents described herein for one or more of the remainder of R^1, R^2, R^3, R^4, R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^i, R^j, R^k, R^m, R^n, R^p, R^r, R^t, R^u, R^w, R^{w2}, R^x, R^z, R^{x2}, R^{S1}, R^{S2}, R^{S3}, R^{S4}, Q^1, Q^2, T^1, T^2, X^1, and X^2.

[00210] In one embodiment, R^1, Q^1, T^1, X^1, R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^{S1}, R^{S2}, R^w, R^{w2}, R^x, R^z, and R^{x2} are each as defined, where applicable, in any of Formula I (including IA, IA', Ia, Ia', Ib and Ib'), Formula II (i.e. including IIa, IIa', IIb, IIb', IIc, IIc', IId, IId', IIe, IIe', IIf and IIf').

[00211] For example, T^1 is $C(=O)NR^aR^b$ and n is 0.

[00212] For example, one of R^a and R^b independently is 5- to 10-membered heteroaryl and the other is hydrogen.

[00213] For example, one of R^a and R^b independently is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, benzimidazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, oxadiazolyl, pyrazolyl, benzodioxolyl, dihydrobenzofuranyl, triazolyl, imidazolyl, furanyl, or thiophenyl, each of which is optionally substituted with one or more groups independently selected from cyano, C_{1-6}haloalkyl, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$NR^{c2}R^{d2}$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, or C_{0-3}alkylene-C_{6-10}aryl.

[00214] For example, one of R^a and R^b independently is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, benzimidazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, oxadiazolyl, pyrazolyl, benzodioxolyl, dihydrobenzofuranyl, triazolyl, imidazolyl, furanyl, or thiophenyl, each of which is optionally substituted with one or more groups independently selected from cyano, $-CF_3$, $-S(=O)_2CH_3$, $-OCH_3$, $-NH_2$, and R^{S6}, in which R^{S6} is CH_3, *i*-propyl, cyclopropyl, cyclopentyl, cyclohexyl, or phenyl.

[00215] For example, one of R^a and R^b is C_{0-1}alkylene-C_{6-10}aryl.

[00216] For example, one of R^a and R^b independently is phenyl, benzyl, naphthyl, or CH_2naphthyl, each of which is optionally substituted with one or more groups independently selected from halo, cyano, CF_3, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$NR^{c2}R^{d2}$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{0-3}alkylene-OR^{e2}, or R^{S7}, in which R^{S7} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, or C_{0-3}alkylene-3- to 12-membered heterocycloalkyl.

[00217] For example, one of R^a and R^b independently is phenyl, $-CH_2$phenyl, naphthyl, or $-CH_2$naphthyl, each of which is optionally substituted with one or more groups independently selected from F, Cl, cyano, $-CF_3$, $-S(=O)_2CH_3$, $-S(=O)_2$i-propyl, $-NHS(=O)_2CH_3$, $-NHS(=O)_2$phenyl, $-N(S(=O)_2CH_3)_2$, $-NHC(=O)CH_3$, $-NHC(=O)OCH_3$, $-OCH_3$, $-OCF_3$, $-O$*i*-propyl, -Ocyclopentyl, $-OCH_2$phenyl, $-NH_2$, $-N(CH_3)_2$,

and R^{S6}, in which R^{S6} is $-CH_3$, $-CH_2OCH_3$, i-propyl, or R^{S7}, in which R^{S7} is cyclopropyl, cyclopentyl, cyclohexyl, phenyl, pyrrolidinyl, or piperidinyl.

[00218] For example, one of R^a and R^b independently is optionally substituted 5- to 9-membered heterocycloalkyl.

[00219] For example, one of R^a and R^b independently is, tetrahydrobenzimidazole, morpholine, tetrahydrofuran, tetrahydropyran, pyrrolidine, piperidine, or piperazine, each of which is optionally substituted with C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, or R^{S6}, in which R^{S6} is C_{1-6}alkyl.

[00220] For example, one of R^a and R^b independently is, tetrahydrobenzimidazole, morpholine, tetrahydrofuran, tetrahydropyran, pyrrolidine, piperidine, or piperazine, each of which is optionally substituted with $-CH_3$, $-C(=O)CH_3$, or -C(=O)Ot-butyl.

[00221] For example, one of R^a and R^b independently is C_{5-6}cycloalkyl and the other is hydrogen.

[00222] For example, each of R^a and R^b independently is cyclohexane or cyclopropane, each of which is optionally substituted with C_{0-3}alkylene-OR^{c2} or C_{0-3}alkylene-$NR^{c2}R^{d2}$.

[00223] For example, each of R^a and R^b independently is cyclohexane or cyclopropane, each of which is optionally substituted with -OH, $-OCH_3$, or $-NH_2$.

[00224] For example, X^1 is optionally substituted C_{0-1}alkylene-C_{6-10}aryl.

[00225] For example, X^1 is phenyl, benzyl, naphthyl, or CH_2naphthyl.

[00226] For example, X^1 is optionally substituted 5 to 10-membered heteroaryl.

[00227] For example, X^1 is benzoxazolyl, benzimidazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, oxadiazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl, each of which can be optionally substituted with one or more substituents selected from oxo.

[00228] For example, X^1 is optionally substituted 5- to 9-membered heterocycloalkyl.

[00229] For example, X^1 is tetrahydrobenzoxazole, tetrahydrobenzimidazole, morpholine, tetrahydrofuran, tetrahydropyran, piperidine, pyrrolidine, or piperazine, each of which can be optionally substituted with one or more substituents independently selected from C_{1-6}alkyl, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$C(=O)OR^e$, or R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{6-10}aryl.

[00230] For example, X^1 is optionally substituted C_{3-6}cycloalkyl.

[00231] For example, X^1 is $-OR^c$ or $-C(=O)C_{1-6}$alkyl.

[00232] For example, X^1 is C_{1-3}alkyl.

[00233] For example, X^1 is $-OCF_3$, $-OC_{1-3}$alkyl, $-NH_2$, -CN, -OH or halo.

[00234] For example, X^1 is C_{0-1}alkylene-$C(=NR^c)NR^cR^d$. For example, X^1 is $-C(=NH)NH_2$.

[00235] For example, X^1 is C_{0-1}alkylene-$NR^cC(=NR^c)NR^cR^d$. For example, X^1 is $-NHC(=NH)NH_2$.

[00236] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$S(=O)_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^n$, and each R^n and R^o is independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl.

[00237] For example, R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or $-OC_{1-6}$alkyl.

[00238] For example, R^2 is H, cyano, methyl or methoxymethyl.

[00239] For example, R^2 is H, methyl or methoxymethyl.

[00240] For example, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, -CN, $-S(=O)_2C_{1-3}$alkyl or $C(=O)OC_{1-3}$alkyl.

[00241] For example, R^3 is -CN, C_{1-3}alkyl, C_{1-3}haloalkyl or $-C(=O)OC_{1-3}$alkyl.

[00242] For example, R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl or $-C(=O)OC_{1-3}$alkyl.

[00243] For example, R^3 is CN, CF_3, methyl or $-C(=O)OC_{1-3}$alkyl.

[00244] For example, R^3 is -CN or $-CF_3$.

[00245] For example, R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, $-S(=O)_2C_{1-3}$alkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$.

[00246] For example, R^4 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3 to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00247] For example, R^4 is C_{3-8}cycloalkyl or C_{6-10}aryl, wherein C_{3-8}cycloalkyl and C_{6-10}aryl are optionally substituted with 1-3 substituents selected from the group consisting of halo,

oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

[00248] For example, R^4 is C_{3-8}cycloalkyl.

[00249] For example, R^4 is cyclopentyl.

[00250] For example, R^4 is C_{6-10}aryl.

[00251] For example, R^4 is phenyl.

[00252] In some embodiments, for a compound of Formula I, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof:

Y is -CR^3= or -N=;

R^1 is Q^1-T^1-$(X^1)_n$;

Q^1 is a bond, -CH_2-, or -CH_2CH_2-;

T^1 is C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, -C(=O)-C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, -NR^aR^b, -$NR^aC(=O)R^a$, -$C(=O)NR^aS(=O)_2R^a$, or -$C(=O)NR^aR^b$;

each X^1 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-$C(=O)OR^c$, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$N^+R^cR^dR^{d'}$, C_{0-3}alkylene-$S(=O)_mR^c$, C_{0-3}alkylene-$NR^cC(=O)R^c$, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-$C(=O)NR^cR^d$, C_{0-3}alkylene-$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, or R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl,

and each R^{S1} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, nitro, oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$NR^eC(=O)R^e$, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-3}alkylene-$C(=O)R^e$, C_{0-3}alkylene-$S(=O)_mR^e$, C_{0-3}alkylene-$NR^eS(=O)_2R^e$, and R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{6-10}aryl or C_{0-3}alkylene-3- to 12-membered heterocycloalkyl,

and each R^{S2} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^w, and -NR^wR^x;

each of R^a and R^b, independently, is H or R^{S5}, in which R^{S5} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl,

and R^{S5} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-

$NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, or C_{0-3}alkylene-3- to 12-membered heterocycloalkyl,

and each R^{S6} is optionally substituted with one or more substituents independently selected from the group consisting of C_{0-3}alkylene-C_{3-8}cycloalkyl C_{0-3}alkylene-$NR^{e2}R^{f2}$, C_{0-3}alkylene-OR^{e2};

R^2 is Q^2-T^2-$(X^2)_p$;

Q^2 is a bond, $-CH_2-$, or $-CH_2CH_2-$;

T^2 is H, halo, cyano, C_{1-6}alkyl, C_{3-8}cycloalkyl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, C(=O)- 3 to 12-membered heterocycloalkyl, $-OR^z$, $-S(=O)_mR^k$, $-P(=O)R^{kk}R^{mm}$, $-NR^kR^m$, $-C(=O)OR^k$ or $-C(=O)NR^kR^m$;

each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-$C(=O)OR^n$ or R^{S3}, in which R^{S3} is C_{1-6}alkyl optionally substituted with C_{0-3}alkylene-OR^p;

each of R^{kk}, and R^{mm}, is independently selected from the group consisting of R^k, $-OR^k$, and $-NR^kR^m$;

each of R^k, and R^m, independently, is H or R^z, in which R^z is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5 to 10-membered heteroaryl:

and each R^z is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{0-3}alkylene-$NR^{n2}R^{o2}$, C_{0-3}alkylene-OR^{n2}, C_{0-3}alkylene-$C(=O)OR^{n2}$, C_{0-3}alkylene-$C(=O)NR^{n2}R^{o2}$, and R^{S11}, in which R^{S11} is C_{0-3}alkylene-3 to 12-membered heterocycloalkyl,

and each R^{S11} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p2}, C_{0-3}alkylene-$S(=O)_mR^{p2}$, C_{0-3}alkylene-$NR^{p2}R^{q2}$, C_{0-3}alkylene-$C(=O)NR^{p2}R^{q2}$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^{p2}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and C_{1-6}haloalkyl;

R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, -CN, $-OR^r$, $-C(=O)R^r$, $-S(=O)_mR^r$, $-NR^rR^t$, or $-C(=O)OR^r$, wherein C_{1-3}alkyl, C_{2-3}alkenyl and C_{2-3}alkynyl are optionally substituted with C_{3-6}cycloalkyl;

R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl, wherein C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5 to 10-membered heteroaryl are optionally

substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$;

each of R^c, R^{c2}, R^d, $R^{d'}$, and R^{d2}, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^e, R^{e2}, R^f, and R^{f2}, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3 to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^n, R^{n2}, R^o, and R^{o2}, independently, is H or R^{S13}, in which R^{S13} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl; and each R^{S13} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p3}, C_{0-3}alkylene-$S(=O)_mR^{p3}$, C_{0-3}alkylene-$NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)OR^{p3}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, and C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^p, R^{p2}, R^{p3}, R^{q2}, and R^{q3}, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each of R^r, and R^t, independently, is H, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^w, R^{w5}, R^x, and R^{x5}, independently, is H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl;

each of n and p independently is 0, 1, 2, 3, 4, or 5, wherein when T^2 is H, p is 0; and m is 0, 1, or 2.

[00253] In one embodiment, for a compound of Formula I, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof:

R^1 is -$(CH_2)_{0-1}$-$C(=O)NR^aR^b$; -CH_2CH_2-NR^aR^b; -CH_2CH_2-$NR^aC(=O)R^a$; -$C(=O)NR^aS(=O)_2R^a$; -$(CH_2)_{0-1}$-C_{6-10}aryl; -$(CH_2)_{0-1}$-5- to 6-membered monocyclic heteroaryl; -$(CH_2)_{0-1}$-9- to 10-membered bicyclic heteroaryl; a 4- to 6-membered monocyclic heterocycloalkyl; a 9- to 10-membered bicyclic heterocycloalkyl; -C(=O)-4- to 6-membered monocyclic heterocycloalkyl; -C(=O)-9- to 10-membered bicyclic heterocycloalkyl; wherein

the aryl, 5heteroaryl, and heterocycloalkyl rings are optionally independently substituted with 1, 2, 3, 4, or 5 X^1;

each X^1 independently is halo; cyano; oxo; C_{1-6}alkyl optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, and C_{0-3}alkylene-4 to 6-membered heterocycloalkyl, wherein heterocycloalkyl is optionally independently substituted with one or more C_{1-6}alkyl; C_{0-3}alkylene-C_{3-6}cycloalkyl optionally substituted with one or more substituents independently selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, and C_{0-3}alkylene-OR^e; C_{0-3}alkylene-C_{6-10}aryl, wherein C_{6-10}aryl is optionally substituted with one or more substituents selected from the group consisting of halo, cyano, nitro, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$C(=O)OR^e$, C_{0-3}alkylene-$C(=O)R^e$, C_{0-3}alkylene-$S(=O)_mR^e$, and C_{0-3}alkylene-$NR^eS(=O)_2R^e$; C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl or 9- or 10-membered bicyclic heterocycloalkyl, wherein heterocycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of oxo, C_{0-3}alkylene-NR^eR^f, and C_{0-3}alkylene-OR^e; C_{0-3}alkylene-5- or 6-membered monocyclic heteroaryl or 9- or 10-membered bicyclic heteroaryl, wherein heteroaryl is independently optionally substituted with one or more C_{0-3}alkylene-OR^e; C_{0-3}alkylene-OR^c; C_{0-3}alkylene-$C(=O)OR^c$; C_{0-3}alkylene-NR^cR^d; C_{0-3}alkylene-$N^+R^cR^dR^{d'}$; C_{0-3}alkylene-$S(=O)_mR^c$; C_{0-3}alkylene-$NR^cC(=O)R^c$; C_{0-3}alkylene-$OC(=O)NR^cR^d$; C_{0-3}alkylene-$C(=O)NR^cR^d$; C_{0-3}alkylene-$C(=NR^c)NR^cR^d$; or C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$;

each of R^a and R^b, independently, is H or R^{S5}, in which R^{S5} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl, C_{0-3}alkylene-9- or 10-membered bicyclic hetercycloalkyl, C_{0-3}alkylene-5- or 6-membered monocyclic heteroaryl, or C_{0-3}alkylene-9- or 10-membered bicyclic heteroaryl;

and R^{S5} is optionally substituted with one or more substituents selected from the group consisting of halo, cyano, oxo, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-$NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-6}cycloalkyl, or C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl;

and each R^{S6} is optionally substituted with one or more C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-$NR^{e2}R^{f2}$, C_{0-3}alkylene-OR^{e2};

R^2 is Q^2-T^2-$(X^2)_p$;

Q^2 is a bond, -CH_2-, or -CH_2CH_2-;

T^2 is H, halo, cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl, 4- to 6-membered monocyclic heterocycloalkyl, 9- or 10-membered bicyclic heterocycloalkyl, 5- or 6-membered monocyclic heteroaryl, 9- or 10-membered bicyclic heteroaryl, C(=O)- 4- to 6-membered monocyclic heterocycloalkyl, -OR^z, -$S(=O)_mR^k$, -$P(=O)R^kR^m$, -NR^kR^m, -$C(=O)OR^k$ or -$C(=O)NR^kR^m$;

each X^2 independently is halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-$C(=O)NR^nR^o$, C_{0-3}alkylene-$C(=O)OR^n$ or C_{1-6}alkyl, wherein C_{1-6}alkyl is optionally substituted with one C_{0-3}alkylene-OR^p;

each of R^{kk}, and R^{mm}, is independently selected from the group consisting of R^k, -OR^k, and -NR^kR^m;

each of R^k, and R^m, independently, is H or R^z, in which R^z is C_{1-6}alkyl, C_{0-3}alkylene-C_{3-6}cycloalkyl, C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl, C_{0-3}alkylene-9- or 10-membered bicyclic heterocycloalkyl, C_{0-3}alkylene-5 or 6-membered monocyclic heteroaryl, or C_{0-3}alkylene-9- or 10-membered bicyclic heteroaryl:

and each R^z is optionally substituted with one or more substituents selected from the group consisting of halo, C_{1-6}alkyl, C_{0-3}alkylene-$NR^{n2}R^{o2}$, C_{0-3}alkylene-OR^{n2}, C_{0-3}alkylene-$C(=O)OR^{n2}$, C_{0-3}alkylene-$C(=O)NR^{n2}R^{o2}$, and R^{S11}, in which R^{S11} is C_{0-3}alkylene-4- to 6-membered monocyclic heterocycloalkyl, C_{0-3}alkylene-9- or 10-membered bicyclic heterocycloalkyl, C_{0-3}alkylene-5- or 6-membered monocyclic heteroaryl, or C_{0-3}alkylene-9- or 10-membered bicyclic heteroaryl;

and each R^{S11} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p2}, C_{0-3}alkylene-$S(=O)_mR^{p2}$, C_{0-3}alkylene-$NR^{p2}R^{q2}$, C_{0-3}alkylene-$C(=O)NR^{p2}R^{q2}$, C_{0-3}alkylene-C_{0-3}alkylene-$C(=O)OR^{p2}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and C_{1-6}haloalkyl;

R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, -CN, -OR^r, -$C(=O)R^r$, -$S(=O)_mR^r$, NR^rR^t, or -$C(=O)OR^r$, wherein C_{1-3}alkyl, C_{2-3}alkenyl and C_{2-3}alkynyl are optionally substituted with C_{3-6}cycloalkyl;

R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, phenyl, or 5- or 6-membered monocyclic heteroaryl, wherein cycloalkyl, phenyl and heteroaryl are optionally substituted

with one or more substituents independently selected from the group consisting of halo, cyano, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, $-OR^{w5}$, and $-NR^{w5}R^{x5}$;

each of R^r, and R^t, independently, is H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, phenyl, 4- to 6-membered monocyclic heterocycloalkyl, or 5- or 6-membered monocyclic heteroaryl;

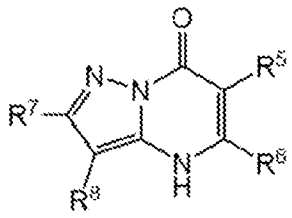
each of R^c, R^{c2}, R^d, $R^{d'}$, R^{d2}, R^e, R^{e2}, R^f, R^{f2}, R^n, R^{n2}, R^o, R^{o2}, R^p, R^{p2}, and R^{q2}, independently, is H, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, phenyl, 4- to 6-membered monocyclic heterocycloalkyl, or 5- or 6--membered monocyclic heteroaryl;

each R^w, R^{w5}, R^x, and R^{x5}, independently, is H, C_{1-3}alkyl, or C_{1-3}haloalkyl;

p is 0, 1, 2, 3, 4, or 5; and

m is 0, 1, or 2.

[00254] In another aspect, the present invention provides the compounds of Formula (III):



(III),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In this formula:

R^5 is selected from the group consisting of $-C(=O)NR^9R^{10}$; $-CH_2C(=O)NR^{11}R^{12}$; $-CH_2CH_2NR^{13}R^{14}$; $-CH_2$-phenyl; $-CH_2$-5-membered monocyclic heteroaryl optionally substituted with one C_{1-3}alkyl, monocyclic C_{5-6}cycloalkyl, or phenyl, wherein phenyl is optionally substituted with one $-OC_{1-3}$alkyl; phenyl optionally substituted with one halo or C_{1-3}alkyl; a 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with 1, 2, or 3 R^{15}; a 5- or 6-membered monocylic heteroaryl optionally substituted with 1, 2, or 3 R^{16}; and 9- or 10-membered bicyclic heteroaryl optionally substituted with 1, 2, 3, or 4 R^{17};

R^9 and R^{10} are independently selected from the group consisting of H; C_{1-3}alkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH and $-OC_{1-3}$alkyl; $-CH_2$phenyl; $-S(=O)_2R^{18}$; C_{5-6}cycloalkyl optionally substituted with one $-NH_2$, oxo, -OH, or $-OC_{1-3}$alkyl; phenyl optionally substituted with 1, 2, or 3 R^{19}; a 5-or 6-membered monocyclic heterocycloalkyl optionally substituted with one $-C_{1-3}$alkyl, $-C(=O)C_{1-3}$alkyl, or $-C(=O)OC_{1-6}$alkyl; a 5- or 6-membered monocyclic heteroaryl optionally substituted with 1, 2, or 3 R^{20}; and a 9- or 10-membered bicyclic heteroaryl optionally substituted with 1 or 2 halo; or

R^9 and R^{10} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one phenyl;

R^{11} and R^{12} are independently selected from the group consisting of H; C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl; phenyl optionally substituted with one -NH_2 or -OC_{1-3}alkyl; and a 5- or 6-membered monocyclic heteroaryl; or R^{11} and R^{12} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one C_{1-3}alkyl, phenyl or -CH_2-phenyl, wherein the phenyl ring of phenyl or -CH_2-phenyl is optionally substituted with one C_{1-3}alkyl;

R^{13} and R^{14} are independently selected from the group consisting of H; -C(=O)C_{1-3}alkyl; -C(=O)phenyl; and phenyl optionally substituted with one -OC_{1-3}alkyl;

each R^{15} is independently selected from the group consisting of oxo; -C(=O)OH; -C(=O)OC_{1-3}alkyl; and C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl;

each R^{16} is independently selected from the group consisting of -CN; -C(=O)OH; -C(=O)OC_{1-3}alkyl; -C(=O)NH_2; -C(=O)NHC_{1-3}alkyl; -C(=O)N(C_{1-3}alkyl)$_2$; -C(=NH)NH_2; -NHC(=NH)NH_2; -NH_2; -NHC_{1-3}alkyl;-N(C_{1-3}alkyl)$_2$; -NHC_{3-6}cycoalkyl; -N(C_{1-3}alkyl)C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, or 5- or 6-membered monocyclic heterocycloalkyl, wherein the monocyclic heterocycloalkyl is optionally substituted with -C_{1-3}alkyl; C_{1-3}haloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH and phenyl; -C_{3-6}cycloalkyl optionally substituted with one -NH_2, C_{1-3}alkyl, C_{1-3}haloalkyl, or -OC_{1-3}alkyl; phenyl optionally substituted with one -OH, -OC_{1-3}alkyl, -NO_2, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of oxo, -OH, -NH_2, -OC_{1-3}alkyl, -C(=O)C_{1-3}alkyl, -S(=O)$_2C_{1-3}$alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OCH_2phenyl, and C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -NH_2, -NHS(=O)$_2C_{1-3}$alkyl, -OH, or -OC_{1-3}alkyl; and 5- or 6-membered monocyclic heteroaryl optionally substituted with one -OH or -OC_{1-3}alkyl;

each R^{17} is independently selected from the group consisting of oxo; halo; -OH; -CN; -NH_2; -NHC_{1-3}alkyl; -N(C_{1-3}alkyl)$_2$; -N^+(C_{1-3}alkyl)$_3$; -NHC(=O)C_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -S(=O)$_m C_{1-3}$alkyl; -C(=O)OH; -C(=O)OC_{1-6}alkyl; -C(=O)NH_2; -C(=O)NHC_{1-3}alkyl; -C(=O)N(C_{1-3}alkyl)$_2$; -OC(=O)NH_2; -OC(=O)NHC_{1-3}alkyl; -OC(=O)N(C_{1-3}alkyl)$_2$; -C(=NH)NH_2; -C(=NH)NHC_{1-3}alkyl; -C(=NH)N(C_{1-3}alkyl)$_2$; -OC_{1-3}haloalkyl; C_{1-3}haloalkyl;

monocyclic C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -$N(C_{1-3}alkyl)_2$; -OC_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, phenyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -C(=O)NH_2, -C(=O)NHC_{1-3}alkyl, -C(=O)$N(C_{1-3}alkyl)_2$, -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)_2$, -$NHC(=O)C_{1-3}$alkyl, or -$NHS(=O)_2C_{1-3}$alkyl; and phenyl optionally substituted with one halo, -CN, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl or -$N(C_{1-3}alkyl)_2$;

R^{18} is selected from the group consisting of C_{1-3}alkyl; monocyclic C_{3-6}cycloalkyl; a 5- or 6-membered monocyclic heteroaryl; phenyl; and -CH_2phenyl; wherein the phenyl ring of phenyl or -CH_2phenyl is optionally substituted with one halo, -CN, or -OC_{1-3}alkyl;

each R^{19} is independently selected from the group consisting of halo; -CN; -NH_2; -NHC_{1-3}alkyl; -$N(C_{1-3}alkyl)_2$; -$NHC(=O)C_{1-3}$alkyl; -$NHS(=O)_2C_{1-3}$alkyl; -$N(S(=O)_2C_{1-3}alkyl)_2$;-$NHS(=O)_2C_{3-6}$cycloalkyl; -$NHS(=O)_2$phenyl; -NHC(=O)OH; -$NHC(=O)OC_{1-3}$alkyl; -$S(=O)_2C_{1-3}$alkyl; -OC_{1-3}alkyl optionally substituted with one phenyl; C_{1-3}haloalkyl; -OC_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; a 5- or 6-membered monocyclic heterocycloalkyl; and C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -$N(C_{1-3}alkyl)_2$;

each R^{20} is independently selected from the group consisting of -CN; -OC_{1-3}alkyl; -$S(=O)_2C_{1-3}$alkyl; C_{1-3}haloalkyl; and C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl; and monocyclic C_{3-6}cycloalkyl;

R^6 is selected from the group consisting of H; halo; -CN; -NH_2; -C(=O)OH; -C(=O)OC_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -$S(=O)_mC_{1-3}$alkyl; -$P(=O)(C_{1-3}alkyl)_2$; -C(=O)$NR^{21}R^{22}$; C_{1-3}haloalkyl; -OC_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -$N(C_{1-3}alkyl)_2$; C_{1-3}alkyl optionally substituted with one -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)_2$, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -$S(=O)_mC_{1-3}$alkyl, -C(=O)C_{1-3}alkyl, -OR^{23}, or 5- or 6-membered monocyclic heteroaryl, wherein monocyclic heteroaryl is optionally substituted with 1 or 2 C_{1-3}alkyl; monocyclic C_{3-6}cycloalkyl optionally substituted with one -C(=O)OH, -C(=O)OC_{1-3}alkyl or C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -OH or -OC_{1-3}alkyl; a 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one -C(=O)OH, or -C(=O)OC_{1-3}alkyl; and a 5- or 6-membered heteroaryl optionally substituted with 1 or 2 C_{1-3}alkyl;

R^{21} and R^{22} are independently selected from the group consisting of H; C_{1-6}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)_2$, or 5- or 6-membered monocyclic heteroaryl;

C_{1-3}haloalkyl optionally substituted with one -OH or -OC_{1-3}alkyl; a 5- or 6-membered monocyclic heteroaryl optionally substituted with 1 or 2 C_{1-3}alkyl; and a 4- to 6-membered monocyclic heterocycloalkyl; or

R^{21} and R^{22} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one -C(=O)OH, -C(=O)OC_{1-3}alkyl, or C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -OH or -OC_{1-3}alkyl;

R^{23} is selected from the group consisting of H; C_{1-3}haloalkyl; C_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -C(=O)NH_2, -C(=O)NHC_{1-3}alkyl, -C(=O)N(C_{1-3}alkyl)$_2$, phenyl, 5- or 6-membered monocyclic heteroaryl, or 5- or 6-membered monocyclic heterocycloalkyl, wherein monocyclic heterocycloalkyl is optionally substituted with 1 or 2 oxo or C_{1-3}alkyl; a 4-, 5-, or 6-membered monocyclic heterocycloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of oxo and C_{1-3}alkyl; and a 5- or 6-membered monocyclic heteroaryl;

R^7 is selected from the group consisting of -CN; -OH; -C(=O)OH; -C(=O)OC_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -S(=O)$_m$$C_{1-3}$alkyl; -$NH_2$; -NH$C_{1-3}$alkyl; -N($C_{1-3}$alkyl)$_2$; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl; C_{1-3}haloalkyl; C_{2-3}alkenyl optionally substituted with one monocyclic C_{3-6}cycloalkyl; C_{2-3}alkyny optionally substituted with one monocyclic C_{3-6}cycloalkyl; monocyclic C_{3-6}cycloalkyl; -O-5- or 6-membered monocyclic heterocycloalkyl; and -OC_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, or -C(=O)OC_{1-3}alkyl;

R^8 is selected from the group consisting of C_{1-3}alkyl; C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; phenyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of -CN, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl and -OC_{1-3}haloalkyl; and pyridinyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of -CN, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl and -OC_{1-3}haloalkyl;

with the proviso that:

a) when R^5 is unsubstituted phenyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl, unsubstituted phenyl, or unsubstituted pyridine;

b) when R^5 is unsubstituted cyclohexyl, R^6 is methyl and R^7 is methyl, R^8 is not unsubstituted pyridine;

c) when R^5 is unsubstituted cyclopentyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl or unsubstituted pyridine,

d) when R^6 is methyl, R^7 is methyl and R^8 is 3,4-di-ethoxy-phenyl, R^5 is not unsubstituted 1-pyrrolidine, unsubstituted 1-piperidine, 4-methyl-1-piperidine, unsubstituted 2-1,2,3,4-tetrahydro-isoquinoline, or unsubstituted morpholine;

e) when R^5 is unsubstituted CH_2-phenyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl, trifluoromethyl, unsubstituted pyridine, unsubstituted phenyl, phenyl mono-substituted with 4-F, 4-Cl, 2-methoxy or 4-methoxy, or phenyl disubstituted with 3,4-methoxy;

f) when R^5 is unsubstituted CH_2-phenyl, R^6 is methyl and R^7 is trifluoromethyl, R^8 is not unsubstituted phenyl or phenyl substituted with 2-Cl or 4-Cl;

g) when R^6 is methyl, R^7 is methyl and R^8 is unsubstituted phenyl, R^5 is not $CH_2CH_2C(=O)NH$-phenyl wherein the phenyl ring is unsubstituted or is substituted at the 4-position with Cl, methyl or methoxy;

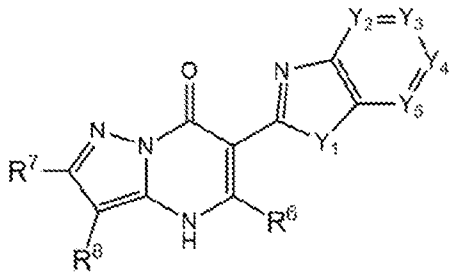
h) when R^6 is methyl or ethyl, R^7 is methyl and R^8 is unsubstituted phenyl, R^5 is not substituted pyrazolo[1,5-*a*]pyrimidin-7-yl;

i) when R^6 is H, R^7 is isopropyl and R^8 is methyl, R^5 is not unsubstituted pyrazole; and

j) the compound is not wherein R^5 is unsubstituted CH_2-phenyl, R^6 is H, R^7 is methyl and R^8 is unsubstituted phenyl.

[00255] In one embodiment of compounds of Formula (III), R^5 is a 9- or 10-membered bicyclic heteroaryl optionally substituted with 1, 2, 3, or 4 R^{17}.

[00256] In one embodiment, a subset of compounds of Formula (III) includes those of Formula (IIIa):



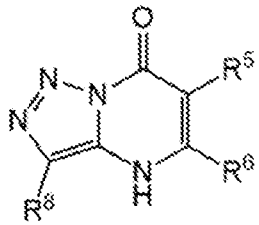
(IIIa),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, wherein Y_1 is -O-, -NH-, -NR^{24}-, or -S-, and Y_2, Y_3, Y_4, and Y_5 are -N= or -CR^{25}=, provided that 0, 1 or 2 of Y_2, Y_3, Y_4, and Y_5 are -N=; wherein R^{24} is selected from the group consisting of C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; and phenyl optionally substituted with one halo, -CN,

C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl or -N(C_{1-3}alkyl)$_2$; and wherein R^{25} is H or R^{17}, wherein R^{17} is as defined for compounds of Formula (III), provided that 0, 1, 2 or 3 of Y_2, Y_3, Y_4, and Y_5 are -CR^{25}= wherein R^{25} is R^{17}; and wherein R^6, R^7 and R^8 are as defined for compounds of Formula (III).

[00257] In one embodiment of compounds of Formula (IIIa), R^6 is -CN or C_{1-3}alkyl optionally substituted with one -NH_2, -NHC_{1-3}alkyl, -N(C_{1-3}alkyl)$_2$, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -S(=O)$_m$$C_{1-3}$alkyl, -C(=O)$C_{1-3}$alkyl, -$OR^{23}$, or 5- or 6-membered monocyclic heteroaryl, wherein monocyclic heteroaryl is optionally substituted with 1 or 2 C_{1-3}alkyl; and R^7 is -CN or -CF_3, wherein R^{23} is as defined for compounds of Formula (III).

[00258] In another aspect, the present invention provides the compounds of Formula (IV):



(IV),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In this formula R^5, R^6, and R^8 are as defined for compounds of Formula (III), and provided the compound is not wherein R^5 is unsubstituted phenyl, R^6 is H and R^8 is 2-fluoro-phenyl.

[00259] Representative compounds of the present invention are listed in Table 1A below followed by their compound number:

Table 1A

N-(4-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1001**);
5-methyl-7-oxo-*N*,3-diphenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1002**);
5-methyl-3-phenyl-6-(4-phenylpiperazine-1-carbonyl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**A1003**);
5-methyl-6-(morpholine-4-carbonyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**A1004**);
5-methyl-7-oxo-3-phenyl-*N*-(pyridin-3-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1005**);

N-(2-aminophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1006**);
5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-*N*-(4-(trifluoromethyl)phenyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1007**);
N-cyclopentyl-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1008**);
5-methyl-3-phenyl-6-(pyrrolidine-1-carbonyl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**A1009**);
N-cyclohexyl-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1010**);
5-methyl-3-phenyl-6-(piperidine-1-carbonyl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**A1011**);
5-methyl-7-oxo-3-phenyl-*N*-(p-tolyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1012**);
N-benzyl-*N*-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1013**);
N-((1*R*,2*R*)-2-aminocyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1014**);
N-(4-cyanophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1015**);
N-(4-chlorophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1016**);
5-methyl-7-oxo-3-phenyl-*N*-(pyridin-2-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1017**);
5-methyl-7-oxo-3-phenyl-*N*-(pyridazin-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1018**);
N-(3,5-dimethylisoxazol-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1019**);
N-(isoxazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1020**);
N-(2-acetamidophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1021**);

5-methyl-*N*-(2-(methylsulfonamido)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1022**);
N-benzyl-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1023**);
5-methyl-7-oxo-3-phenyl-*N*-(pyrazin-2-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1024**);
5-methyl-7-oxo-3-phenyl-*N*-(tetrahydro-2*H*-pyran-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1025**);
5-methyl-*N*-(1-methylpiperidin-4-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1026**);
N-(1-acetylpiperidin-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1027**);
5-methyl-7-oxo-3-phenyl-*N*-(thiazol-2-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1028**);
5-methyl-*N*-(1-methyl-1*H*-pyrazol-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1029**);
N-(3-chlorophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1030**);
N-(2-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1031**);
N-(3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1032**);
N-(2-chlorophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1033**);
tert-butyl (*S*)-3-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamido)pyrrolidine-1-carboxylate (**A1034**);
(*S*)-5-methyl-7-oxo-3-phenyl-*N*-(pyrrolidin-3-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1035**);
N-(2-cyanophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1036**);
5-methyl-7-oxo-3-phenyl-*N*-(o-tolyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1037**);

methyl (2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamido)phenyl)carbamate (**A1038**);
N-(3-acetamidophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1039**);
5-methyl-7-oxo-3-phenyl-*N*-(1*H*-1,2,4-triazol-3-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1040**);
N-(1-cyclohexyl-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1041**);
5-(methoxymethyl)-*N*-(2-methoxyphenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1042**);
N-(2,3-dimethoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1043**);
N-(2-(cyclopentyloxy)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1044**);
5-methyl-*N*-(3-(methylsulfonamido)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1045**);
5-methyl-*N*-(3-(*N*-(methylsulfonyl)methylsulfonamido)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1046**);
5-methyl-7-oxo-3-phenyl-*N*-(pyridin-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1047**);
N-(4-isopropyloxazol-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1048**);
5-methyl-7-oxo-3-phenyl-*N*-(2-(trifluoromethoxy)phenyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1049**);
5-methyl-7-oxo-3-phenyl-*N*-(3-(trifluoromethoxy)phenyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1050**);
N-(2-(isopropylsulfonyl)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1051**);
3-cyclopentyl-N-(2-methoxyphenyl)-5-methyl-7-oxo-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1052**);
N-(2-(dimethylamino)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1053**);

5-methyl-7-oxo-3-phenyl-*N*-(2-(pyrrolidin-1-yl)phenyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1054**);
5-methyl-7-oxo-3-phenyl-*N*-(2-(piperidin-1-yl)phenyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1055**);
N-(4,5-dimethyloxazol-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1056**);
N-(2-methoxyphenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1057**);
N-(4-isopropyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1058**);
5-methyl-7-oxo-3-phenyl-*N*-(2-(phenylsulfonamido)phenyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1059**);
N-(2-isopropoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1060**);
N-(4-cyclopentyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1061**);
N-(2,2-difluorobenzo[*d*][1,3]dioxol-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1062**);
N-(4-methoxypyridin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1063**);
N-(6-methoxypyridin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1064**);
N-(1-isopropyl-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1065**);
N-(3-isopropoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1066**);
N-(3,5-dimethoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1067**);
5-methyl-7-oxo-3-phenyl-*N*-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1068**);
N-(3-aminophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1069**);

N-(3-cyanophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1070**);
N-(5-fluoro-2-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1071**);
N-(2-(methoxymethyl)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1072**);
N-(1,3-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1073**);
5-methyl-*N*-(oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1074**);
5-methyl-*N*-(5-methyloxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1075**);
5-methyl-7-oxo-3-phenyl-*N*-(1*H*-pyrazol-3-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1076**);
5-methyl-*N*-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1077**);
5-methyl-*N*-(1-methyl-1*H*-pyrazol-5-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1078**);
N-(1,5-dimethyl-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1079**);
N-(4,5-difluoro-2-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1080**);
5-methyl-*N*-(3-methyl-1*H*-pyrazol-5-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1081**);
N-(3-(cyclopentyloxy)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1082**);
5-methyl-*N*-(2-(methylsulfonyl)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1083**);
5-methyl-*N*-(3-(methylsulfonyl)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1084**);
N-(2-methoxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (diastereomer 1) (**A1085**);

N-(3-(benzyloxy)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1086**);
N-(2-methoxypyridin-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1087**);
N-(6-methoxypyridin-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1088**);
N-(2-methoxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (diastereomer 2) (**A1089**);
N-(4-cyano-1-methyl-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1090**);
N-((1*S*,2*S*)-2-hydroxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1091**);
N-((1*S*,2*R*)-2-hydroxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1092**);
N-(2-methoxypyridin-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1093**);
N-(5-methoxypyridin-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1094**);
N-(4-cyclopropylthiazol-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1095**);
5-methyl-*N*-(2-(methylsulfonyl)pyridin-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1096**);
N-(3-methoxypyrazin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1097**);
N-(6-methoxypyrazin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1098**);
N-(3-methoxypyridin-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1099**);
N-(3-methoxypyridin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-6-carboxamide (**A1100**);
N-(2,3-dihydrobenzofuran-7-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1101**);

N-(2,3-dihydrobenzofuran-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1102**);
N-(4-methoxypyridin-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1103**);
N-(4-methoxypyrimidin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1104**);
N-(4-methoxypyridin-2-yl)-2,5-dimethyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1105**);
2,5-dimethyl-*N*-(2-(methylsulfonyl)phenyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1106**);
N-(chroman-8-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1107**);
5-methyl-*N*-(5-(methylsulfonyl)pyridin-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1108**);
5-methyl-*N*-(4-(methylsulfonyl)pyridin-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1109**);
N-(6-methoxypyridazin-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1110**);
5-methyl-7-oxo-3-phenyl-*N*-(propylsulfonyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1111**);
N-(benzylsulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1112**);
5-methyl-*N*-(6-(methylsulfonyl)pyridin-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1113**);
N-(3-methoxyphenyl)-*N*,5-dimethyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1114**);
N-(1-(2-methoxyethyl)-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1115**);
5-methyl-7-oxo-3-phenyl-*N*-(phenylsulfonyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1116**);
5-methyl-*N*-(methylsulfonyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1117**);

N-(1-(2-hydroxyethyl)-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1118**);
N-(2-(cyclohexanesulfonamido)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1119**);
5-methyl-7-oxo-3-phenyl-*N*-(pyridin-2-ylsulfonyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1120**);
N-((2-methoxyphenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1121**);
N-(3-methoxyphenyl)-5-methyl-2-(methylthio)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1122**);
2-cyclopropyl-*N*-(3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1123**);
N-(cyclohexylsulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1124**);
N-((3-methoxyphenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1125**);
N-(3-methoxyphenyl)-5-methyl-2-(methylsulfonyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1126**);
N-((2-chlorophenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1127**);
N-((3-cyanophenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1128**);
N-(3-bromo-5-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1129**);
N-(3-bromo-2-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1130**);
N-(2-bromo-3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1131**);
N-((3-methoxybenzyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1132**);
N-(3-fluoro-5-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1133**);

N-(3-chloro-5-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1134**);
N-(2-chloro-3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1135**);
N-(2-fluoro-3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1136**);
N-(3-fluoro-2-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1137**);
N-(3-chloro-2-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1138**);
N-(3-bromo-5-((dimethylamino)methyl)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1139**);
5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1140**);
N-(2-hydroxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1141**);
5-methyl-7-oxo-*N*-(2-oxocyclohexyl)-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1142**);
(*S*)-*N*-(1-hydroxy-3-methoxypropan-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1143**);
2-cyano-*N*-(6-methoxypyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1144**);
N-(2-aminophenyl)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetamide (**B1001**);
5-methyl-6-(2-morpholino-2-oxoethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1002**);
N-(2-methoxyethyl)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetamide (**B1003**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-*N*-(pyridin-4-yl)acetamide (**B1004**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-*N*-phenylacetamide (**B1005**);

N-(4-methoxyphenyl)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetamide (**B1006**);
5-methyl-6-(2-oxo-2-(4-phenylpiperazin-1-yl)ethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1007**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-N-(pyridin-3-yl)acetamide (**B1008**);
5-methyl-6-(2-(4-(4-methylbenzyl)piperazin-1-yl)-2-oxoethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1009**);
N-(2-methoxyphenyl)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetamide (**B1010**);
N-(3-methoxyphenyl)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetamide (**B1011**);
6-(2-aminoethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1012**);
N-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)ethyl)acetamide (**B1013**);
N-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)ethyl)benzamide (**B1014**);
6-(2-((3-methoxyphenyl)amino)ethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1015**);
5-methyl-3-phenyl-6-(pyridin-4-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1001**);
5-methyl-3-phenyl-6-(*m*-tolyl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1002**);
5-methyl-3-phenyl-6-(pyridin-3-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1003**);
6-(3-chlorophenyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1004**);
6-(1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1005**);
6-(imidazo[1,2-*a*]pyridin-6-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1006**);

5-methyl-3-phenyl-6-(quinolin-3-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1007**);
6-(7-amino-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1008**);
N-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1*H*-benzo[*d*]imidazol-7-yl)acetamide (**C1009**);
6-(5-cyclopentyloxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1010**);
6-(benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1011**);
6-(5-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1012**);
6-(5-cyclopentyloxazol-2-yl)-5-(methoxymethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1013**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1014**);
5-methyl-3-phenyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1015**);
6-(5-methoxy-1H-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1016**);
5-methyl-3-phenyl-6-(4,5,6,7-tetrahydro-1H-benzo[*d*]imidazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1017**);
6-(4-methoxy-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1018**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1019**);
5-methyl-6-(5-methyl-4*H*-1,2,4-triazol-3-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1020**);
6-(4,5-dimethyl-1*H*-imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1021**);
6-(7-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1022**);

3-isopropyl-5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2(3*H*)-one (**C1023**);
5-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1024**);
8-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1025**);
6-(7-methoxy-1*H*-indazol-3-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1026**);
5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)oxazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1027**);
6-(5-chlorobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1028**);
5,5'-bis(methoxymethyl)-3,3'-diphenyl-2,2'-bis(trifluoromethyl)-[6,6'-bipyrazolo[1,5-*a*]pyrimidine]-7,7'(4*H*,4'*H*)-dione (**C1029**);
5-methyl-6-(oxazolo[4,5-b]pyridin-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1030**);
2,5-dimethyl-3-phenyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1032**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-6,7-dihydrobenzo[d]oxazol-4(5*H*)-one (**C1033**);
5-methyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-3-(*m*-tolyl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1034**);
3-(3-fluorophenyl)-5-methyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1035**);
5-methyl-3-(pyridin-3-yl)-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1036**);
6-(4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1037**);
6-(4-ethoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1038**);
6-(4-isopropoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1039**);

6-(4-bromobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1040**);
6-(4-(2-methoxyethoxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1041**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-2,5-dimethyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1042**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carboxylic acid (**C1043**);
6-(8-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1044**);
6-(4-(cyclopropylmethoxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1045**);
6-(4-ethylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1046**);
5-methyl-6-(4-(methylthio)benzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1047**);
6-(4-methoxy-4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1048**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(*1H*,*4H*)-dione (**C1049**);
2-(difluoromethyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1050**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1051**);
6-(4-hydroxy-4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1052**);
6-(4-hydroxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1053**);
5-methyl-6-(4-(methylsulfonyl)benzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1054**);
6-(4-chlorobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1055**);

6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(methoxymethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1056**);
6-(5-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1057**);
6-(7-methoxyoxazolo[5,4-*b*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1058**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-5,6,7,8-tetrahydro-4*H*-oxazolo[4,5-*c*]azepin-4-one (**C1059**);
5-methyl-6-(4-methylbenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1060**);
6-(4-(2-aminoethoxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1061**);
N-(2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl)oxy)ethyl)acetamide (**C1062**);
2-amino-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1063**);
2-methoxy-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1064**);
6-(7-methoxy-1-methyl-1*H*-benzo[d]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1065**);
N-(2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl)oxy)ethyl)methanesulfonamide (**C1066**);
5-(2-(dimethylamino)ethoxy)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1067**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-2-(methylsulfonyl)-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1068**);
6-(4-methoxybenzo[*d*]thiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1070**);
5-chloro-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1071**);
2-((6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-2-yl)oxy)acetic acid (**C1072**);

6-(4-(benzyloxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1073**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazole-4-carboxamide (**C1074**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazole-4-carbonitrile (**C1075**);
6-(4-fluorobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1076**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2,5-bis(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1077**);
6-(4-(dimethylamino)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1078**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1079**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-((tetrahydro-2*H*-pyran-4-yl)oxy)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1080**);
6-(7-bromo-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1081**);
6-(5-bromo-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1082**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-2-(2-methoxyethoxy)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1083**);
5-methoxy-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1084**);
5-amino-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1085**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-(2-methoxyphenyl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1086**);
6-(4-methoxy-1-methyl-1*H*-benzo[d]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1087**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl dimethylcarbamate (**C1088**);

6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carbonitrile (**C1089**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carboxylic acid (**C1090**);
3-(2-fluorophenyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1091**);
6-(4-methoxy-7-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1092**);
6-(4-methoxy-5-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1093**);
6-(7-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1094**);
6-(5-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1095**);
6-(7-methoxyoxazolo[5,4-*c*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1096**);
5-methyl-6-(4-(methylsulfinyl)benzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1097**);
6-(4-methoxy-6-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1098**);
5-((benzyloxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1099**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazole-7-carbonitrile (**C1100**);
ethyl 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazole-4-carboxylate (**C1101**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazole-4-carboxamide (**C1102**);
5-(hydroxymethyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1103**);
6-(4-(hydroxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1104**);

6-(6-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1105**);
5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazolo[4,5-*c*]pyridin-4(5*H*)-one (**C1106**);
3-(4-fluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1107**);
6-(4-(methoxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1108**);
5-((dimethylamino)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1109**);
6-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1110**);
6-(7-acetyl-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1111**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carbonitrile (**C1112**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-7-carboxamide (**C1113**);
3-(3-fluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1114**);
6-(4-methoxybenzo[d]oxazol-2-yl)-3-(4-methoxyphenyl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1115**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazolo[4,5-c]pyridin-4(5H)-one (**C1116**);
2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-4-yl)oxy)acetic acid (**C1117**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-5-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1118**);
3-(3,5-difluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1119**);
6-(4-methoxybenzo[d]oxazol-2-yl)-3-(3-methoxyphenyl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1120**);

6-(4-methoxybenzo[d]oxazol-2-yl)-5-(methylthio)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1121**);
2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-4-yl)oxy)acetamide (**C1122**);
6-(6-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1123**);
6-(4-methoxy-7-(methylsulfonyl)benzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1125**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-5-carbonitrile (**C1126**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-(pyridin-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1127**);
6-(6-(aminomethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1128**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-(pyridin-3-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1129**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid (**C1130**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid (**C1131**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1132**);
3-(2,6-difluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1133**);
6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1134**);
6-(6-(aminomethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (HCl salt) (**C1135**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylthio)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1136**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylsulfinyl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1137**);

6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylsulfonyl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1138**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1139**);
ethyl 2-(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)acetate (**C1140**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboximidamide (**C1141**);
6-(4-methoxybenzo[d]oxazol-2-yl)-N-(2-methoxyethyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1142**);
6-(4-(hydroxymethyl)-5-isopropyloxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1143**);
5-acetyl-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1144**);
6-(6-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1145**);
2-((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)acetic acid (**C1146**);
2-(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)acetic acid (**C1147**);
2-(6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-3-yl)benzonitrile (**C1148**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboxamide (**C1149**);
N-(7-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazolo[5,4-d]pyrimidin-5-yl)acetamide (**C1150**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((2-methoxyethoxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1151**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((oxetan-3-yloxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1152**);
6-(5-isopropyl-4-(methoxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1153**);

6-(7-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1154**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboxylic acid (**C1155**);
6-(6-aminobenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1156**);
6-(5-cyclohexyl-4-(hydroxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1157**);
6-(5-cyclohexyl-4-(methoxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1158**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(((2-oxopyrrolidin-3-yl)oxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1159**);
6-(6-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1160**);
6-(4-methoxy-6-(methylamino)benzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1161**);
6-(6-(dimethylamino)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1162**);
4-methoxy-N,N,N-trimethyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-6-aminium (**C1163**);
4-(6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-3-yl)benzonitrile (**C1164**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazole-4-carboxylic acid (**C1165**);
6-(6-(hydroxymethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1166**);
6-(4-methoxyoxazolo[4,5-c]pyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1167**);
5-methyl-6-(3-oxo-1,3-dihydroisobenzofuran-1-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1168**);
5-cyclohexyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazole-4-carboxylic acid (**C1169**);

5-methyl-6-(oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1170**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-4-(m-tolyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1171**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-(m-tolyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1172**);
3-(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)propanoic acid (**C1173**);
6-(5-amino-7-methoxyoxazolo[5,4-d]pyrimidin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1174**);
6-(6-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1175**);
6-(1-cyclohexyl-4-methoxy-1H-benzo[d]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1176**);
5-(((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)methyl)oxazolidin-2-one (**C1177**);
N-(2-hydroxyethyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1178**);
6-(4-methoxybenzo[d]oxazol-2-yl)-N-(2-methoxyethyl)-N-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1179**);
5-((1H-imidazol-1-yl)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1180**);
6-(5-aminobenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1181**);
5-(((1H-imidazol-5-yl)methoxy)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1182**);
5-ethyl-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1183**);
(R)-6-(4-(methoxymethyl)-4,5-dihydrooxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1184**);
6-(4-methoxybenzo[d]oxazol-2-yl)-N-(oxetan-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1185**);

6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-5-(piperidine-1-carbonyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1186**);
methyl (S)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylate (**C1187**);
6-(4-ethylbenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1188**);
6-(1-(cyclopropylmethyl)-4-methoxy-1H-benzo[d]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1189**);
6-(1-cyclohexyl-1H-benzo[d]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1190**);
6-(7-(aminomethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1191**);
(S)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1192**);
6-(6-aminobenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1193**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-N-(tetrahydro-2H-pyran-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1194**);
(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carbonyl)glycine (**C1195**);
(S)-N-(1-hydroxypropan-2-yl)-6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1196**);
N-(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carbonyl)-N-methylglycine (**C1197**);
2-((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)acetamide (**C1198**);
2-((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)-N-methylacetamide (**C1199**);
6-(4-methoxy-1-(2-methoxyethyl)-1H-benzo[d]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1200**);
6-(1-(2-hydroxyethyl)-4-methoxy-1H-benzo[d]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1201**);

6-(6-amino-7-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1202**);
6-(6-(hydroxymethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1203**);
5-methyl-6-(4-(methylthio)benzo[d]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1204**);
6-(7-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1205**);
6-(5-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1206**);
(R)-5-(2-(hydroxymethyl)pyrrolidine-1-carbonyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1207**);
(S)-N-(1-hydroxy-3-methylbutan-2-yl)-6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1208**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-N-(3,3,3-trifluoro-2-hydroxypropyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1209**);
2-acetyl-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1210**);
2-ethynyl-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1211**);
N-(2-(dimethylamino)ethyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1212**);
(4*R*,5*S*)-5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1213**);
5-methyl-6-(1-oxoisoindolin-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1214**);
6-(3-(hydroxymethyl)-8-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1215**);
(5*S*)-5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1216**);
6-(6-amino-1-oxoisoindolin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1217**);

6-(6-amino-4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1218**);
N-(2-hydroxy-2-methylpropyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1219**);
6-(4-methoxy-1-oxoisoindolin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1220**);
2-(4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1*H*-benzo[d]imidazol-1-yl)acetic acid (**C1221**);
6-(benzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1222**);
6-(4-aminobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1223**);
6-(7-(hydroxymethyl)-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1224**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(((1-methyl-2-oxopyrrolidin-3-yl)oxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1225**);
5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1226**);
6-(6-amino-4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1227**);
2-(cyclopropylethynyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1228**);
5-methyl-3-phenyl-6-(1-phenyl-1*H*-benzo[*d*]imidazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1229**);
6-(7-aminobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1230**);
5-methyl-3-phenyl-6-(1-(2,2,2-trifluoroethyl)-1H-benzo[*d*]imidazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1231**);
5-((2,2-difluoroethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1232**);
ethyl 4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohex-3-ene-1-carboxylate (**C1233**);

4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohex-3-ene-1-carboxylic acid (**C1234**);
6-(1-(cyclopentylmethyl)-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1235**);
5-(3-(hydroxymethyl)cyclopentyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1236**);
4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohexane-1-carboxylic acid (Isomer 1) (**C1237**);
4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohexane-1-carboxylic acid (Isomer 2) (**C1238**);
3-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclopentane-1-carboxylic acid (**C1239**);
6-(6-(1-hydroxyethyl)-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1240**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-vinylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1241**);
2-cyclopropyl-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1242**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-((2-methoxyethoxy)methyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1243**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-*N*-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1244**);
N-((1*H*-pyrazol-3-yl)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1245**);
5-(methoxymethyl)-6-(4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1246**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2(3*H*)-one (**C1247**);
5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1248**);
2-cyano-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxylic acid (**C1249**);

6-(5-amino-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1250**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-5-(((2-oxooxazolidin-5-yl)methoxy)methyl)-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1251**);
3-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclobutane-1-carboxylic acid (**C1252**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(3-methylisoxazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1253**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-5-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4*H*)-one (**C1254**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1255**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-*N*-(1-methyl-1*H*-pyrazol-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1256**);
1-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)piperidine-3-carboxylic acid (**C1257**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-morpholino-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1258**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-((oxetan-3-yloxy)methyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1259**);
6-(5-isopropyloxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1260**);
6-(4-(difluoromethoxy)benzo[*d*]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1261**);
5-(methoxymethyl)-7-oxo-3-phenyl-6-(4-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1262**);
5-((2-methoxyethoxy)methyl)-7-oxo-3-phenyl-6-(4-(2,2,2-trifluoroethyl)oxazolo[4,5-*c*]pyridin-2-yl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1263**);
6-benzyl-3-cyclopropyl-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1264**);
3-cyclopropyl-5-methyl-6-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1265**);

3-cyclopentyl-5-methyl-6-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1266**);
6-benzyl-3-cyclopentyl-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1267**);
6-benzyl-3-isopropyl-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1268**);
3-isopropyl-5-methyl-6-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1269**);
5-methyl-6-(oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1270**);
6-(6-amino-7-chlorobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1271**);
6-(4-(dimethylamino)benzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1272**);
5-methyl-7-oxo-3,6-diphenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1273**);
5-methyl-6-(4-(methylamino)benzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1274**);
5-methyl-6-(oxazolo[4,5-*c*]pyridin-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1275**);
6-(1-cyclohexyl-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1276**);
6-(4-cyclopropoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1277**);
5-methyl-3-phenyl-6-(5-(pyridin-3-yl)-4*H*-1,2,4-triazol-3-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1278**);
6-(6-amino-1-cyclohexyl-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1279**);
5-methyl-7-oxo-3-phenyl-6-(piperidin-1-yl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1280**);
6-(isoxazol-4-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1281**);

5-methyl-6-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1282**);
3-(3-fluorophenyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1283**);
5-(dimethylphosphoryl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1284**);
5-methyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1001**);
6-(5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1002**);
6-(5-cyclopentyl-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1003**);
6-(5-cyclohexyl-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1004**);
6-(5-isopropyl-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1005**);
6-(5-cyclohexyl-1,3,4-thiadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1006**);
6-(5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1007**);
5-methyl-3-phenyl-6-(5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1008**);
5-methyl-6-(5-morpholino-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1009**);
5-methyl-3-phenyl-6-(5-phenyl-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1011**);
5-methyl-3-phenyl-6-(5-(tetrahydrofuran-2-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1012**);
5-methyl-3-phenyl-6-(5-(tetrahydrofuran-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1013**);
5-methyl-3-phenyl-6-(5-(pyrrolidin-1-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1014**);

5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1015**);
5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-4-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1016**);
6-(5-cyclohexyl-1,3,4-oxadiazol-2-yl)-3-cyclopentyl-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1017**);
6-(5-cyclopentyl-1,3,4-oxadiazol-2-yl)-5-(methoxymethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1018**);
6-(5-(methoxymethyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1019**);
5-methyl-3-phenyl-6-(5-(piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1020**);
6-(5-(3-methoxycyclohexyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1021**);
5-methyl-6-(5-(2-methylpyrrolidin-1-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1022**);
5-methyl-6-(5-(1-methylcyclopentyl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1023**);
5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-2-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1024**);
(*S*)-5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1025**);
(*R*)-5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1026**);
6-(5-(3-methoxypiperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1027**);
(*S*)-5-methyl-3-phenyl-6-(5-(2,2,2-trifluoro-1-methoxy-1-phenylethyl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1028**);
(*R*)-5-methyl-3-phenyl-6-(5-(2,2,2-trifluoro-1-methoxy-1-phenylethyl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1029**);
2,5-dimethyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1030**);

tert-butyl 3-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)piperidine-1-carboxylate (**D1031**);
5-methyl-6-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1032**);
6-((5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl)methyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1033**);
6-((5-cyclopentyl-1,3,4-oxadiazol-2-yl)methyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1034**);
6-((5-cyclohexyl-1,3,4-oxadiazol-2-yl)methyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1035**);
5-methyl-3-phenyl-6-(5-(piperidin-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1036**);
6-(5-(3-methoxypyrrolidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1037**);
5-methyl-3-phenyl-2-(trifluoromethyl)-6-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1038**);
benzyl 3-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)morpholine-4-carboxylate (**D1039**);
5-methyl-6-(5-(1-(methylsulfonyl)piperidin-3-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1040**);
6-(5-(1-acetylpiperidin-3-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1041**);
5-methyl-6-(5-(morpholin-3-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1042**);
6-(5-(cyclohexyl(methyl)amino)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1043**);
tert-butyl 4-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)piperidine-1-carboxylate (**D1044**);
tert-butyl 2-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)piperidine-1-carboxylate (**D1045**);
6-(5-(2-methoxycyclohexyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (Isomers 1, 2 and 3) (**D1046**);

5-methyl-6-(5-(4-(methylsulfonyl)morpholin-3-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1047**);
6-(5-(2-methoxypropan-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1048**);
6-(5-(2-methoxycyclopentyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (Isomers 1 and 2) (**D1049**);
6-(5-(4-acetylmorpholin-3-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1050**);
5-methyl-6-(5-(3-methyltetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1051**);
5-methyl-3-phenyl-6-(5-(piperidin-4-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1052**);
5-methyl-6-(5-(1-(methylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1053**);
6-(5-(1-acetylpiperidin-4-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1054**);
6-(5-(1-methoxycyclopentyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1055**);
5-methyl-6-(5-(1-(methylsulfonyl)piperidin-2-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1056**);
6-(5-(1-acetylpiperidin-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1057**);
5-methyl-6-(5-(4-methylpiperazin-1-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1058**);
6-(5-(2-(methoxymethyl)pyrrolidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1059**);
6-(5-(2-(methoxymethyl)piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1060**);
5-methyl-6-(5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1061**);
6-(5-(1-aminocyclopentyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1062**);

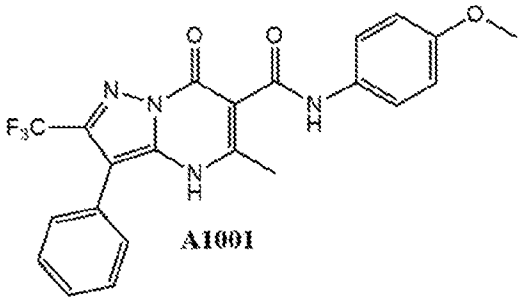
5-methyl-3-phenyl-6-(5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1063**);
6-(5-(2-methoxypyridin-3-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1064**);
5-methyl-6-(5-((1-methylpiperidin-4-yl)methyl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1065**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazole-2-carboxamide (**D1066**);
6-(5-(2-hydroxypyridin-3-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1067**);
6-(5-(1,1-dioxidothiomorpholino)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1068**);
6-(5-(2-(2-aminoethyl)piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1069**);
6-(5-(2-(aminomethyl)piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1070**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazole-2-carbonitrile (**D1071**);
5-methyl-3-phenyl-6-(5-(1,4,5,6-tetrahydropyrimidin-2-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1072**);
N-(2-(1-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)piperidin-2-yl)ethyl)methanesulfonamide (**D1073**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazole-2-carboximidamide (**D1074**);
6-(5-amino-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1075**);
6-(5-(4-methoxypyrimidin-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1076**);
1-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)guanidine (**D1077**);
6-(5-(4-hydroxypyrimidin-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1078**);

6-(5-(3-aminophenyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1079**);
6-(5-(2-aminocyclohexyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1080**);
6-(5-(4-aminophenyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1081**);
6-(5-(2-aminophenyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1082**);
6-(5-(3-(aminomethyl)piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1083**);
6-(5-(3-aminopiperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1084**);
6-(5-(2-hydroxypyridin-4-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1085**);
6-(5-(6-hydroxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1086**);
6-(5-(3-hydroxypiperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1087**);
5-(methoxymethyl)-7-oxo-3-phenyl-6-(5-(piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**D1088**);
6-(5-cyclohexyl-1,3,4-oxadiazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**D1089**); and
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**E1001**);

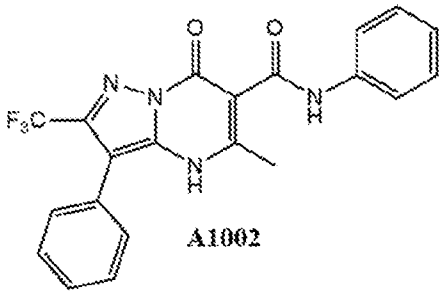
or a pharmaceutically acceptable salt, solvate or hydrate thereof.

[00260] The representative compounds have the following structures as shown in Table 1B below:

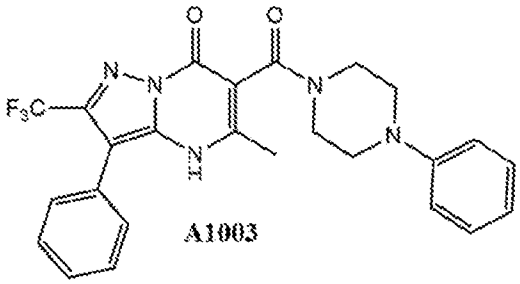
Table 1B



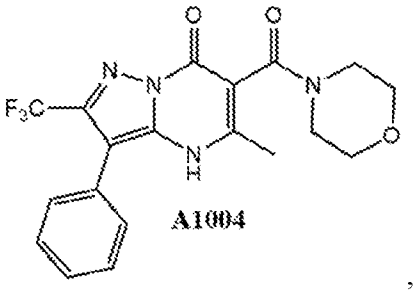
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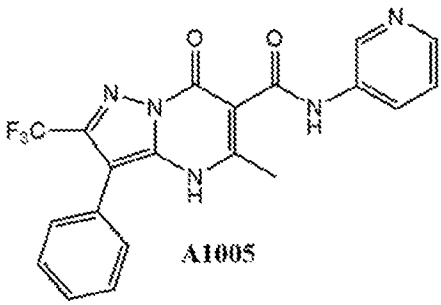
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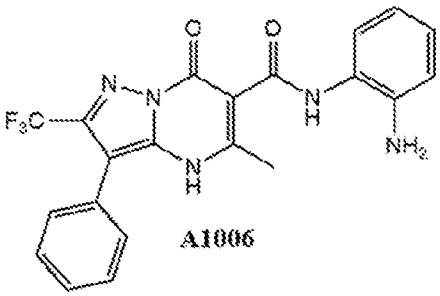
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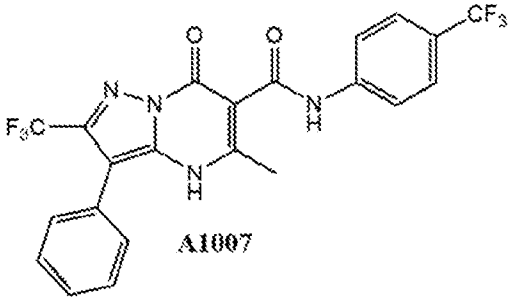
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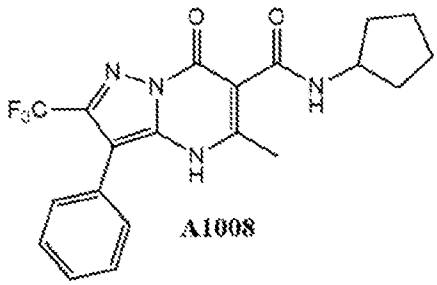
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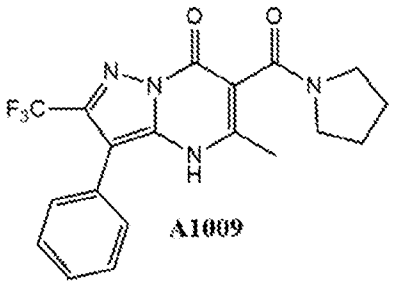
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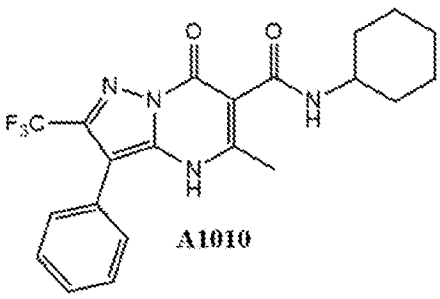
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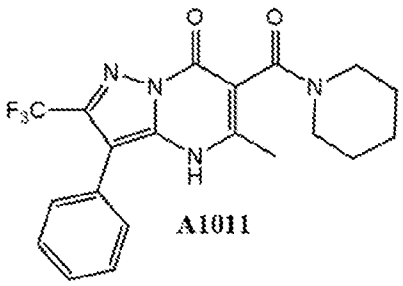
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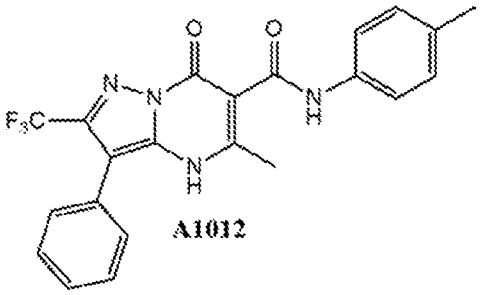
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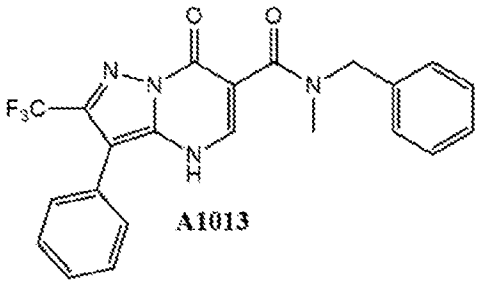
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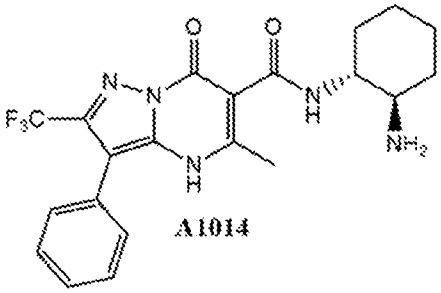
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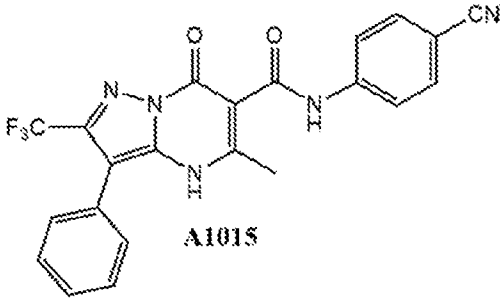
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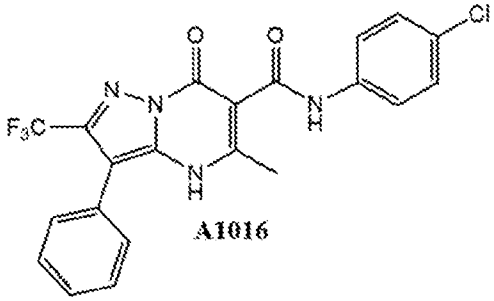
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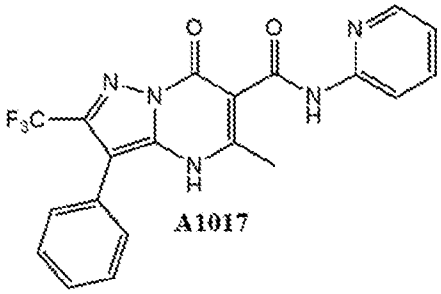
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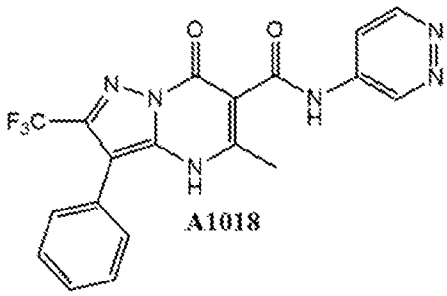
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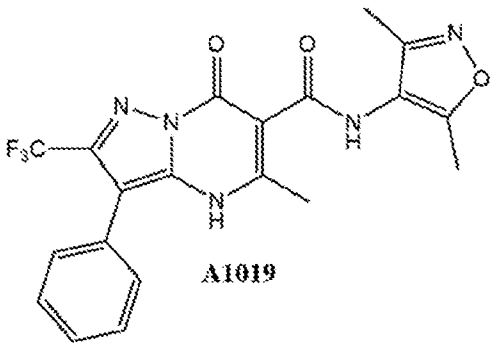
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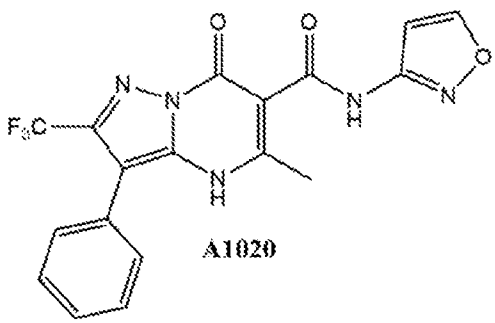
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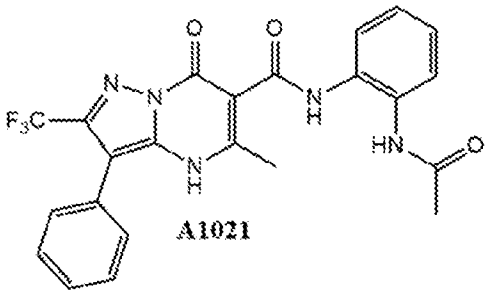
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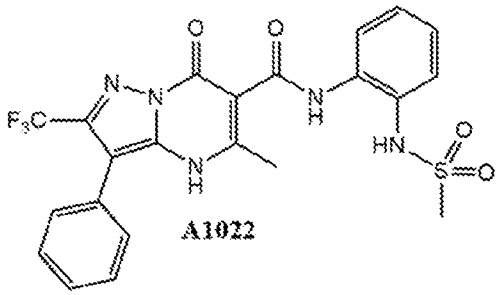
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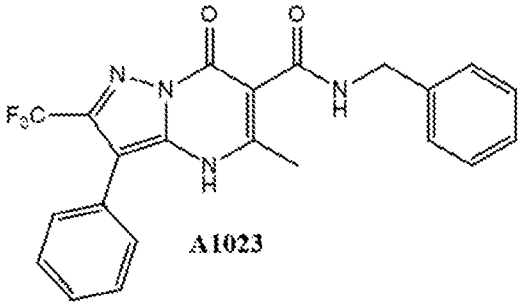
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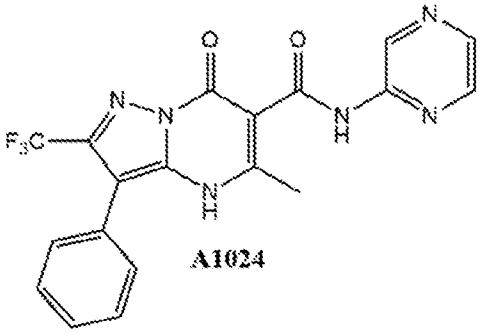
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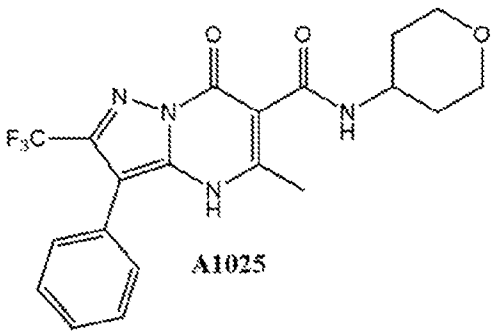
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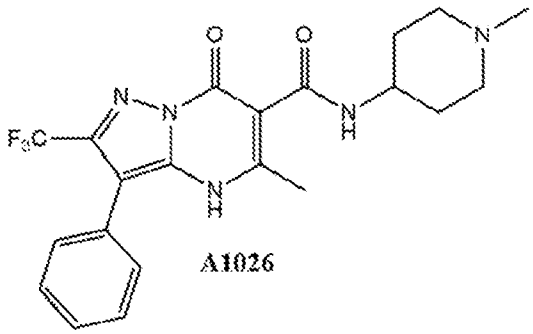
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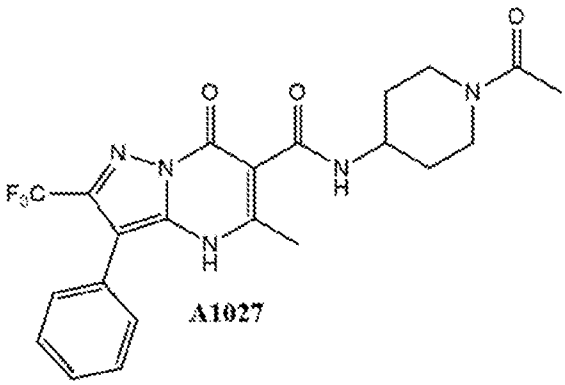
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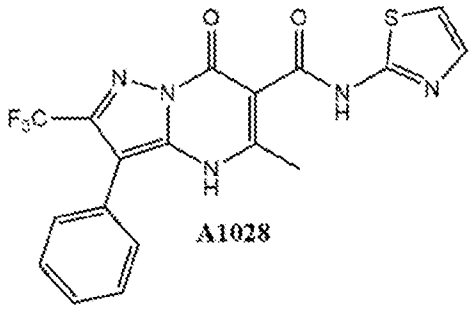
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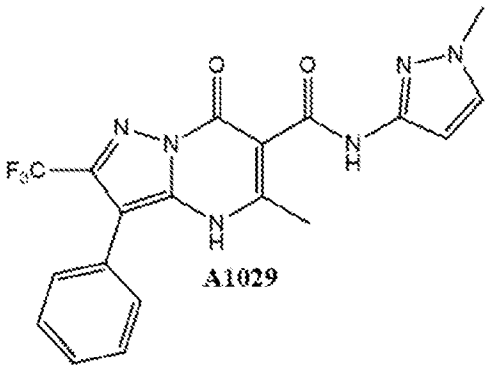
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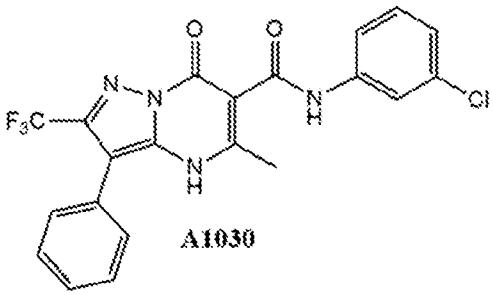
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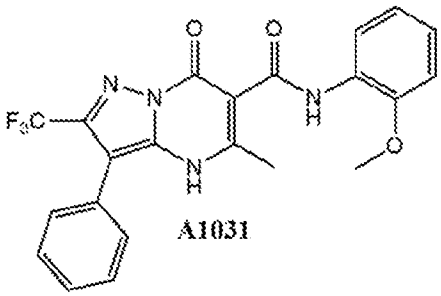
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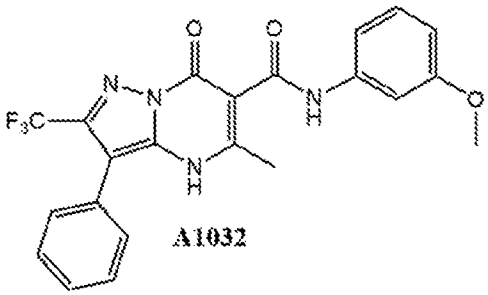
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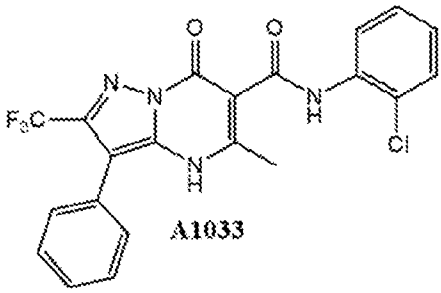
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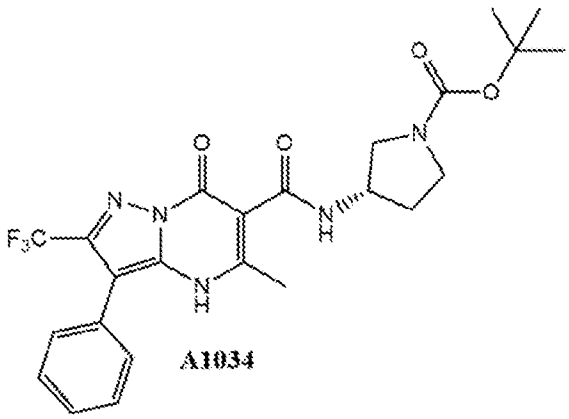
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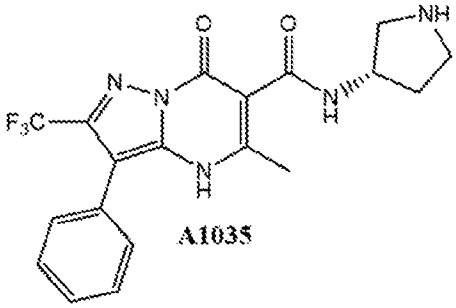
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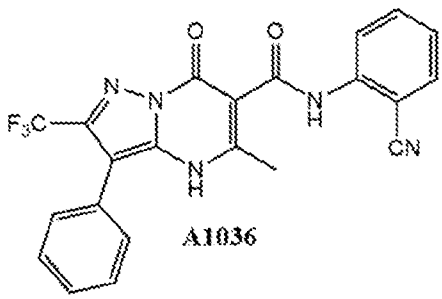
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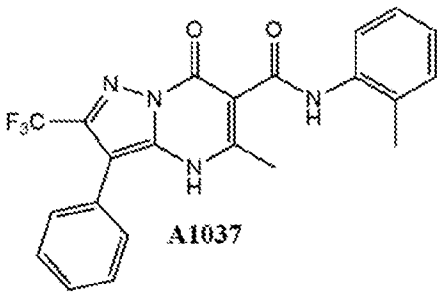
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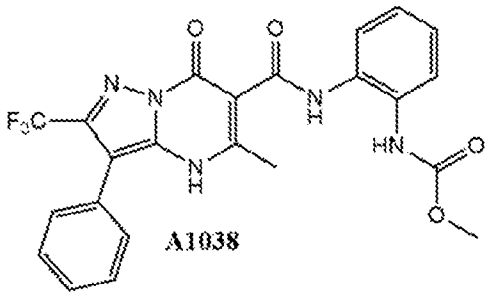
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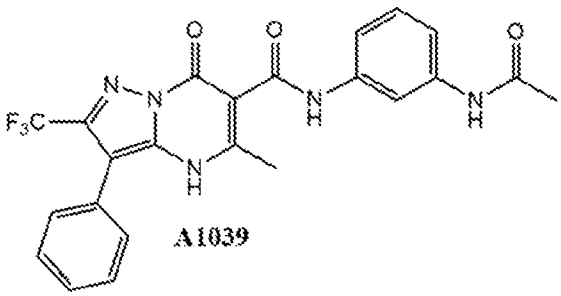
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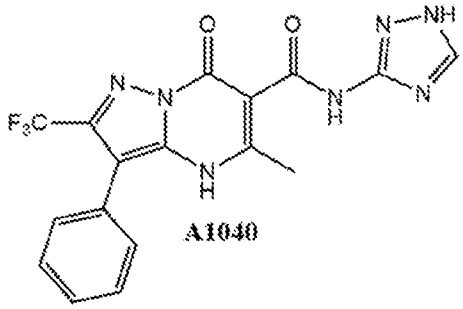
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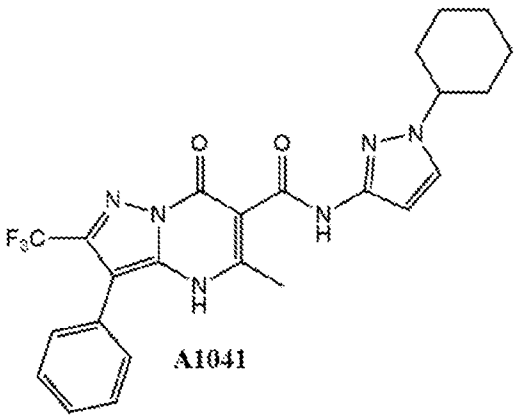
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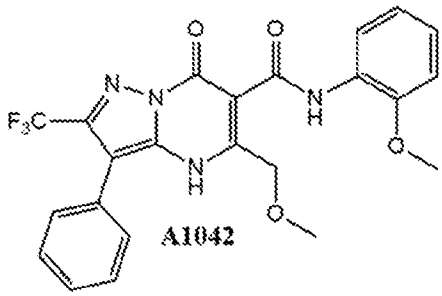
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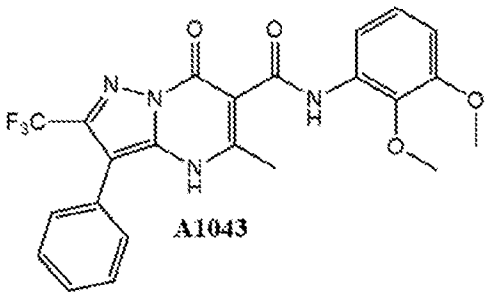
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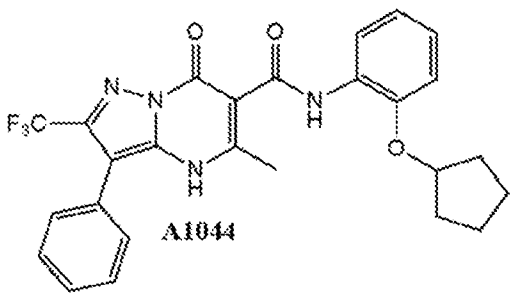
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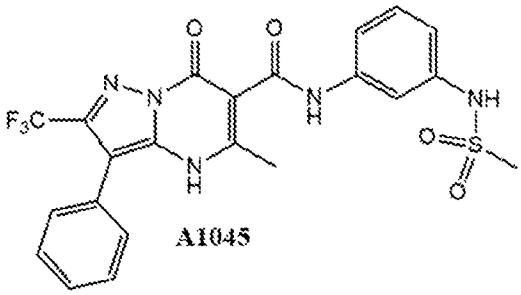
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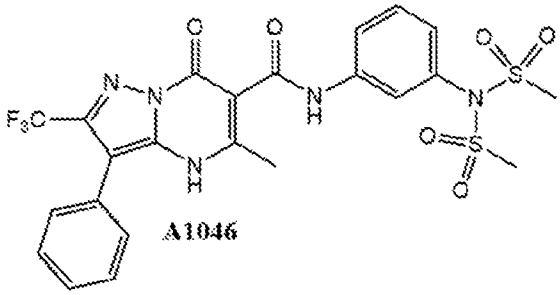
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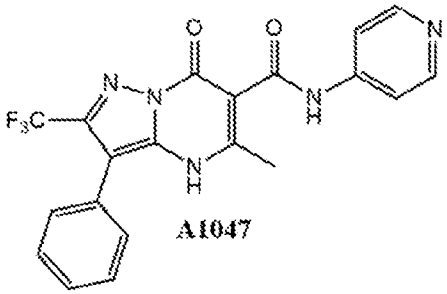
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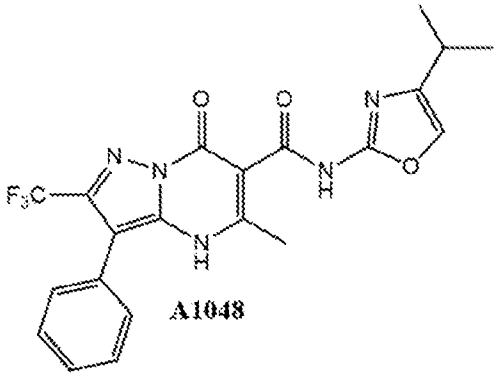
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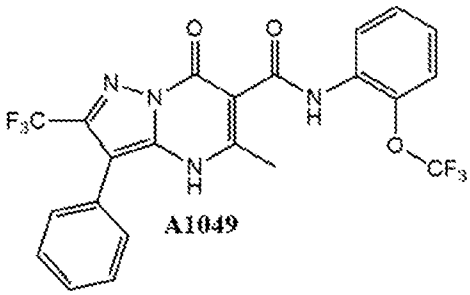
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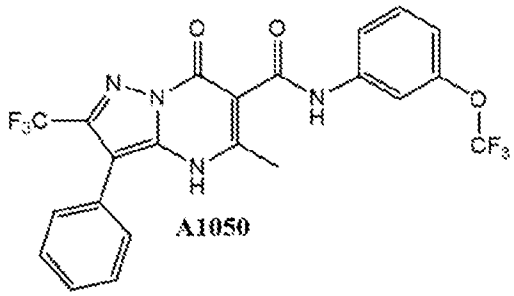
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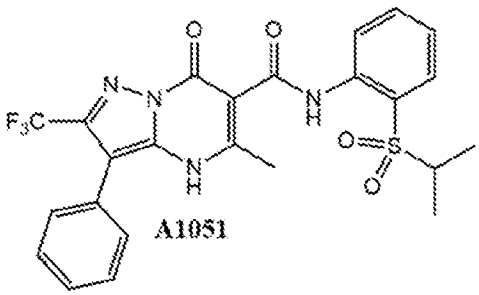
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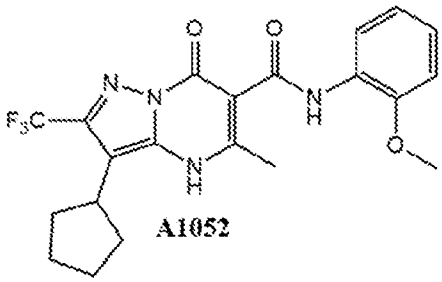
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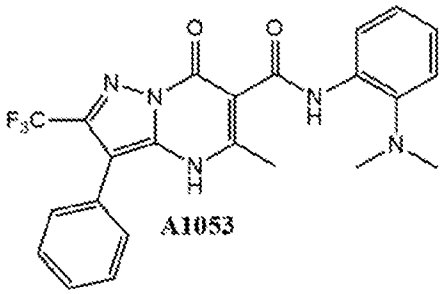
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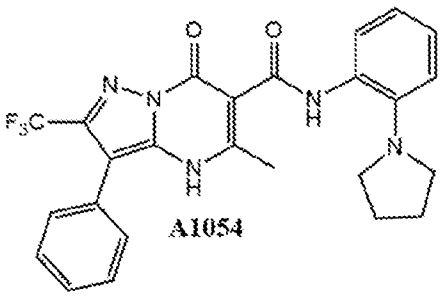
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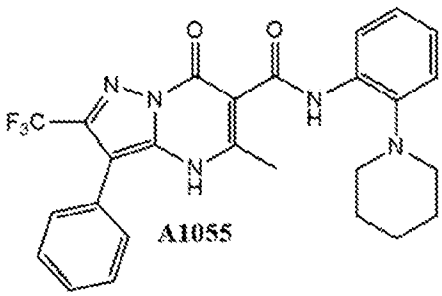
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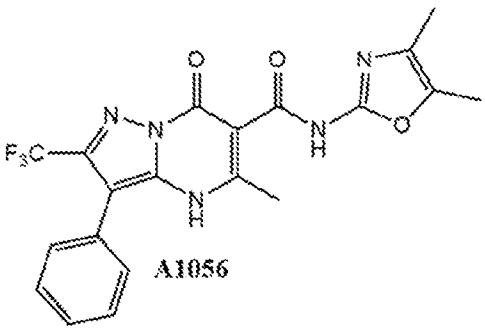
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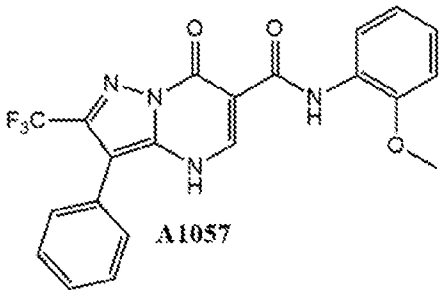
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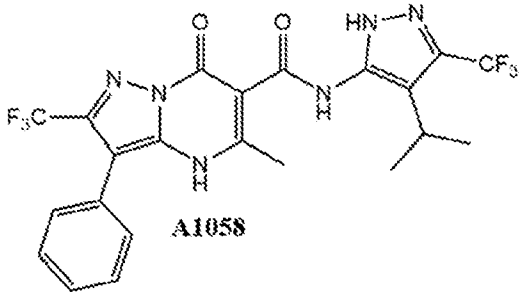
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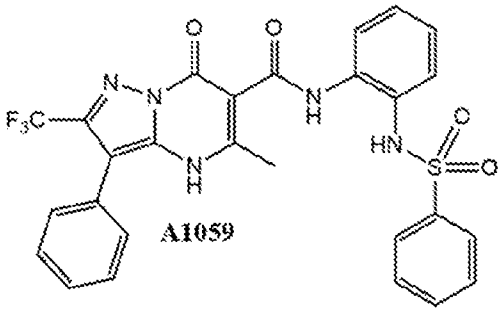
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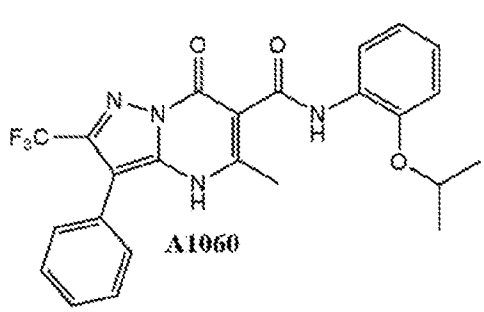
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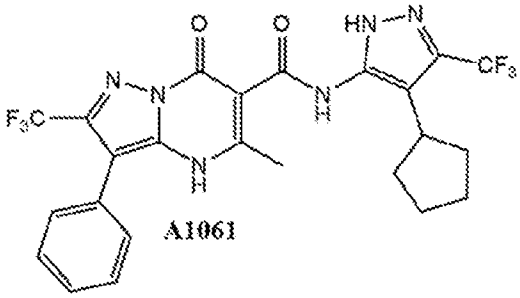
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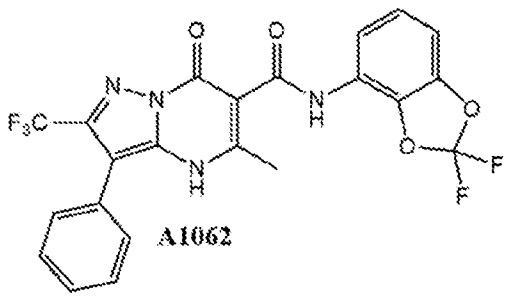
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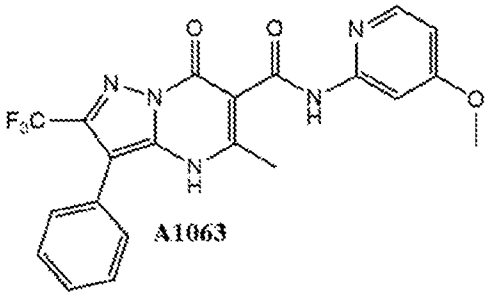
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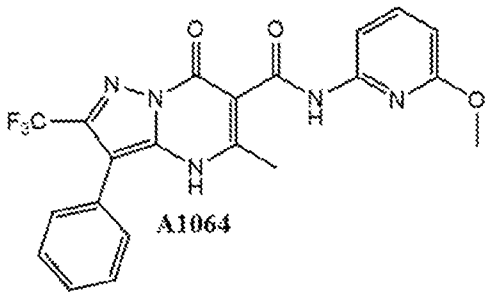
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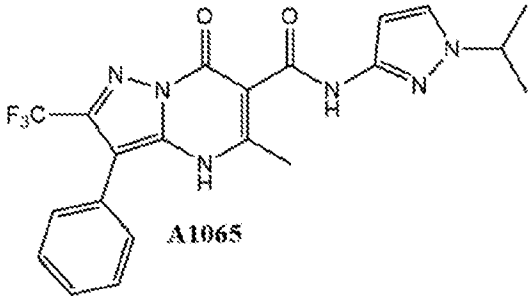
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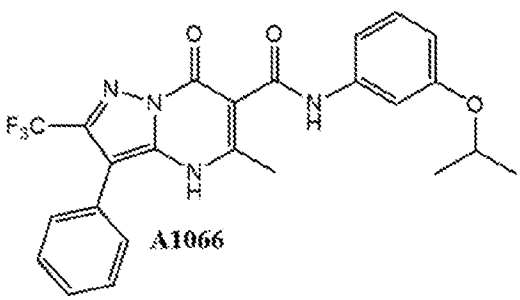
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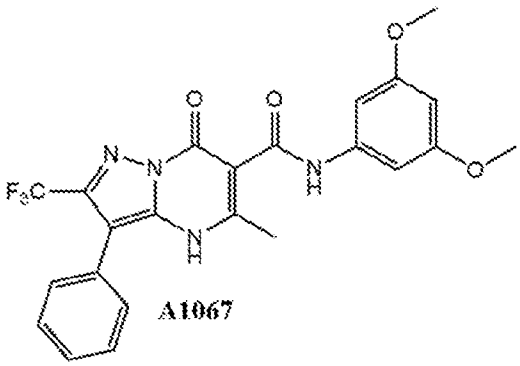
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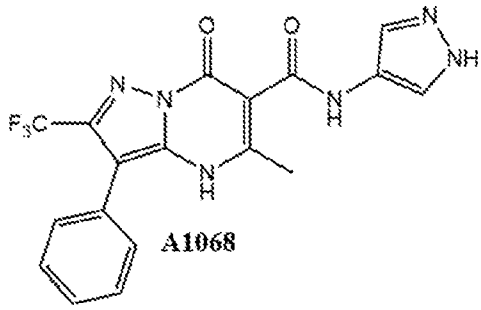
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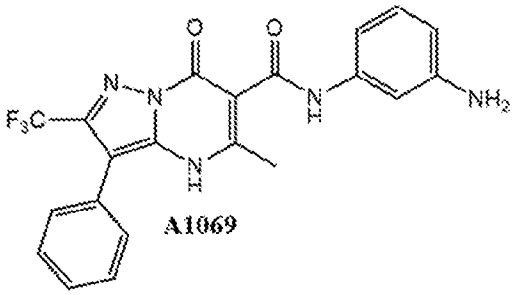
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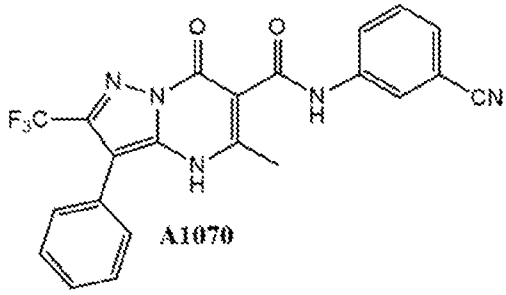
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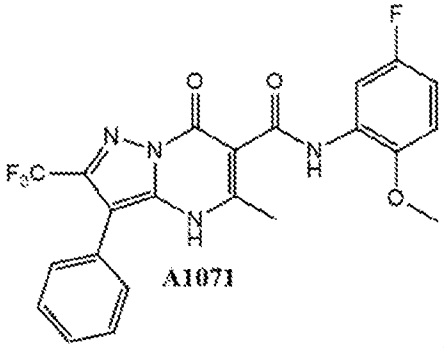
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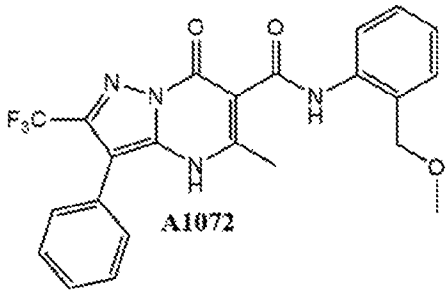
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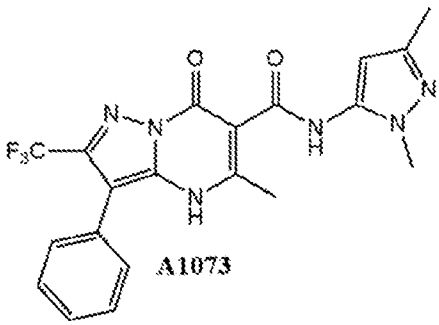
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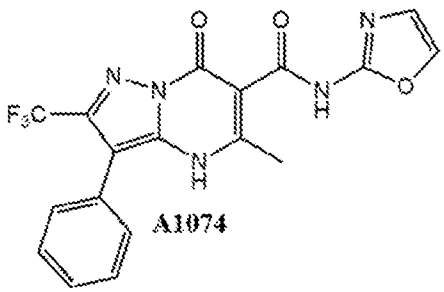
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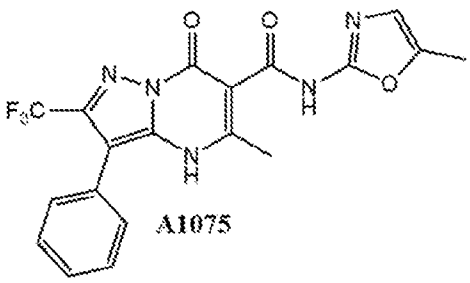
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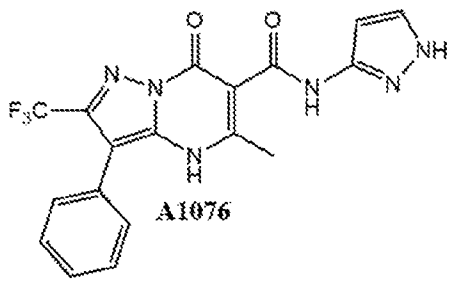
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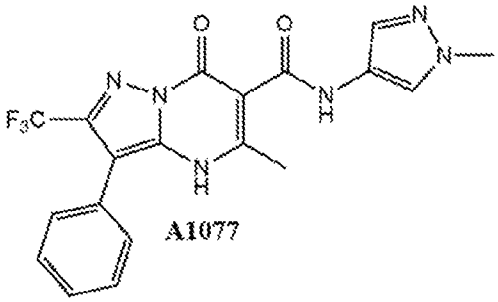
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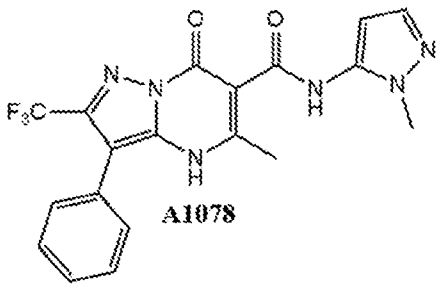
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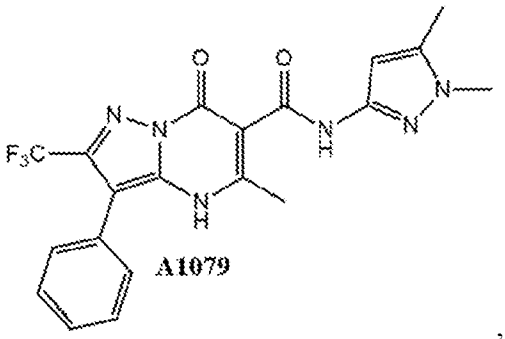
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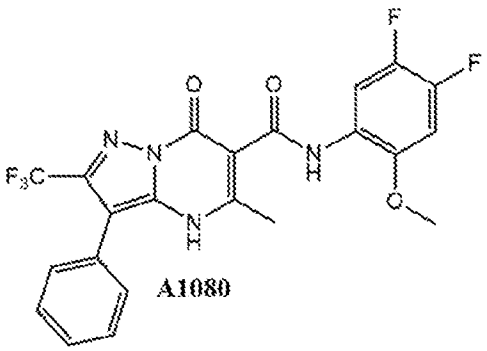
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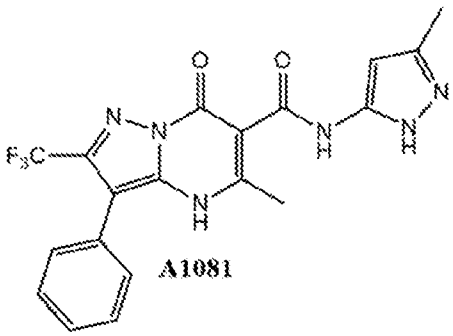
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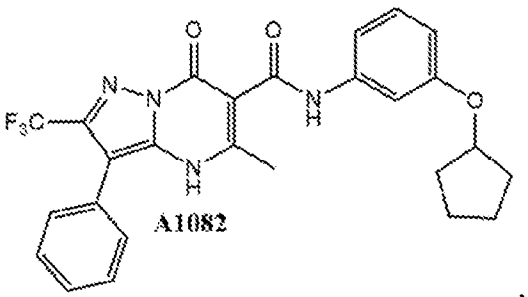
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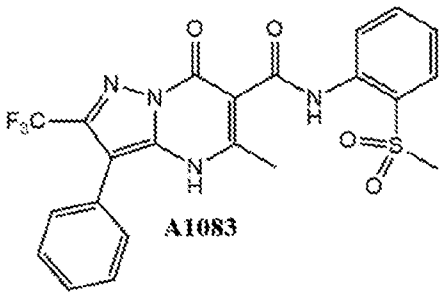
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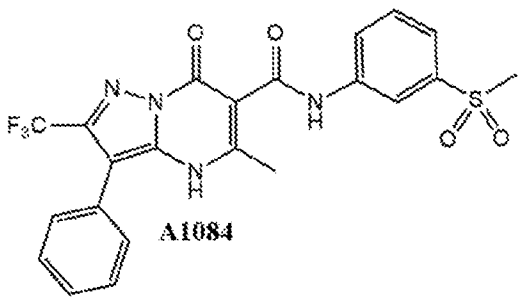
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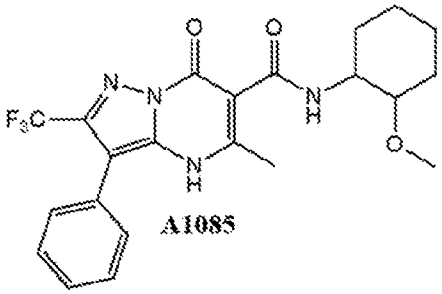
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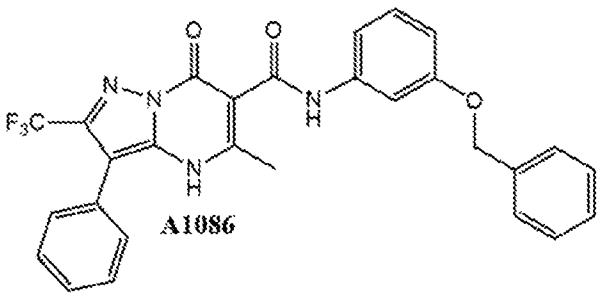
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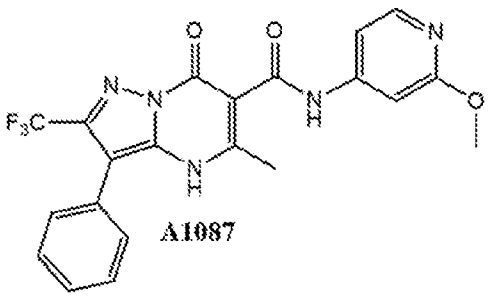
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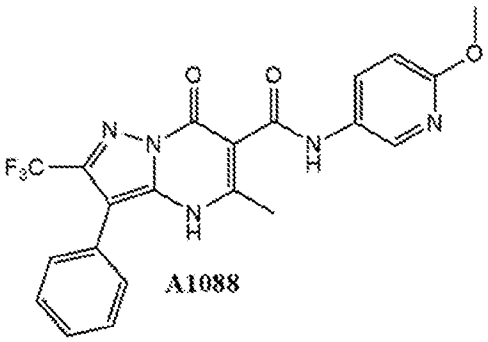
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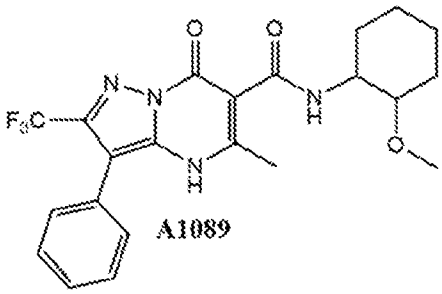
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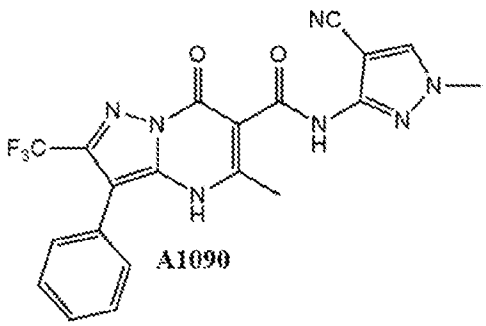
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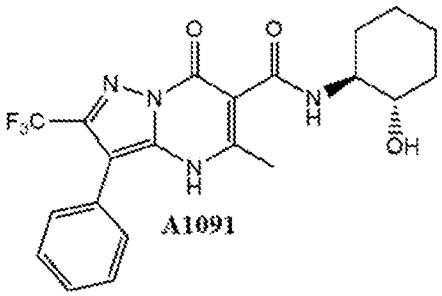
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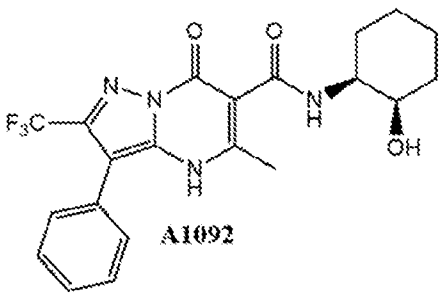
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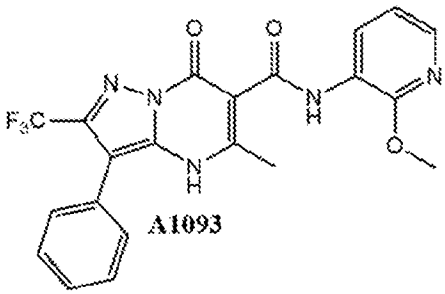
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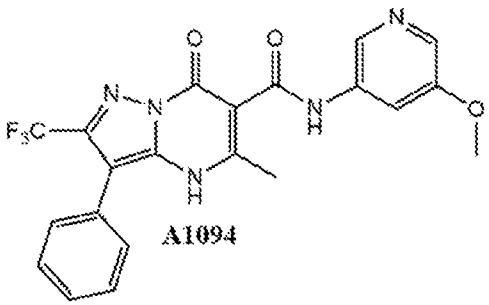
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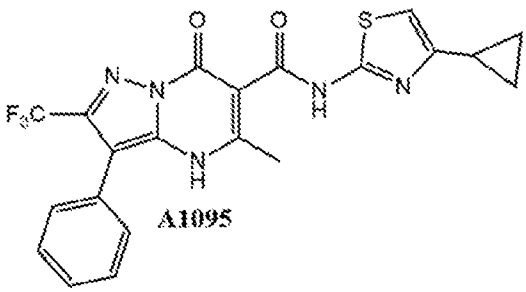
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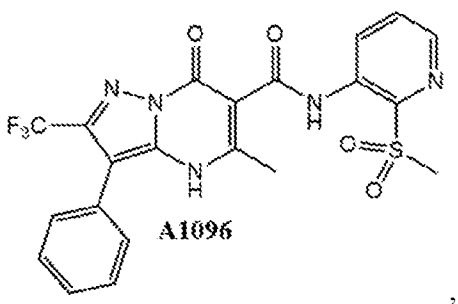
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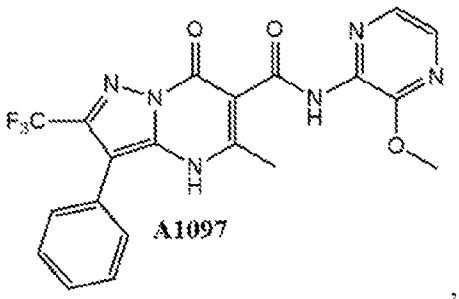
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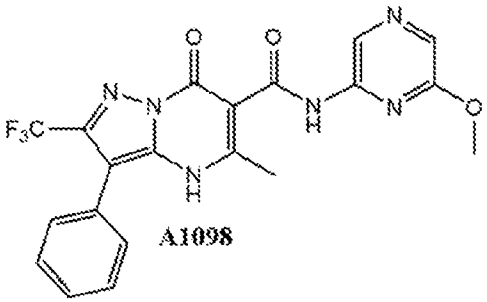


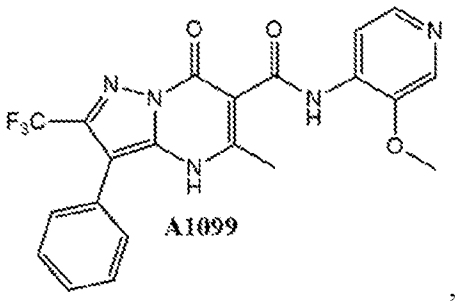
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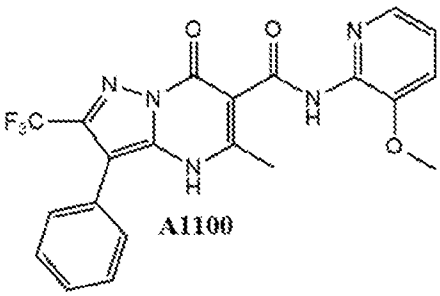


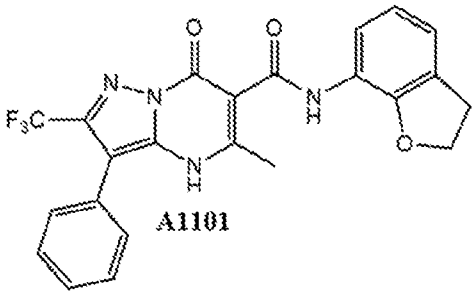
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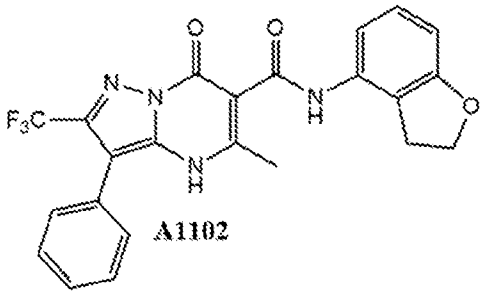

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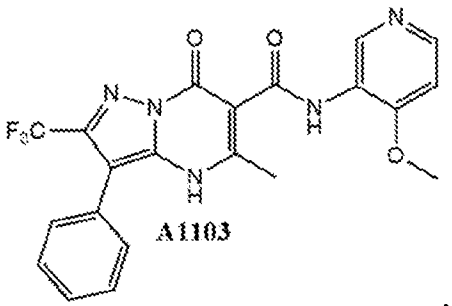

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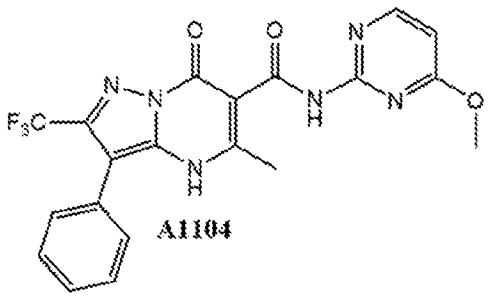

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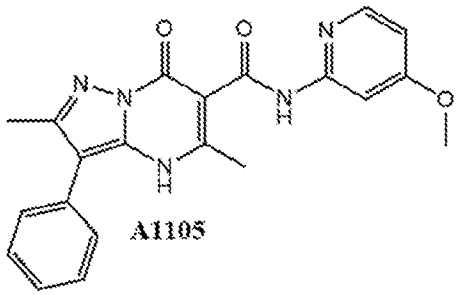

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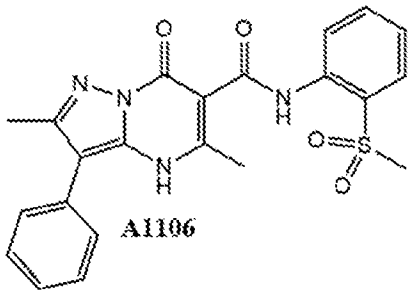

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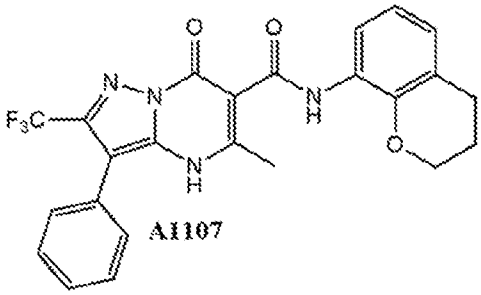

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A1103

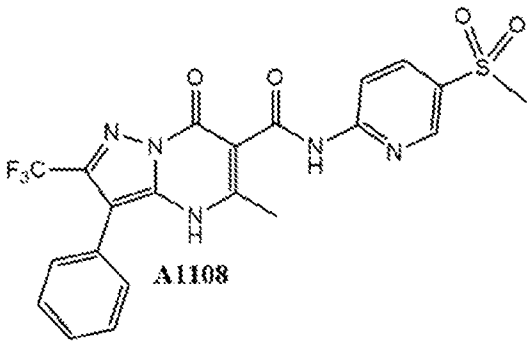

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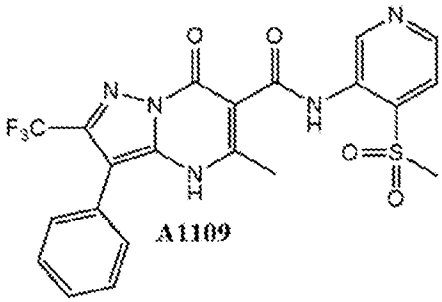

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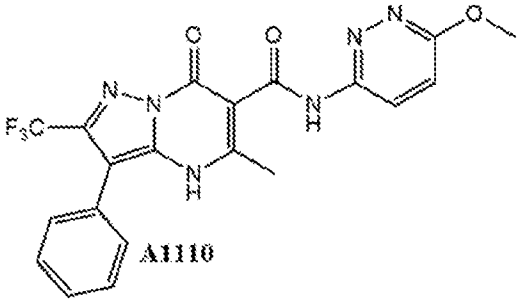
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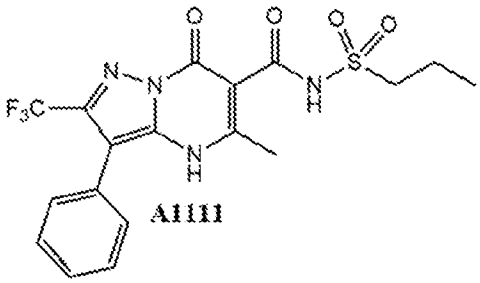
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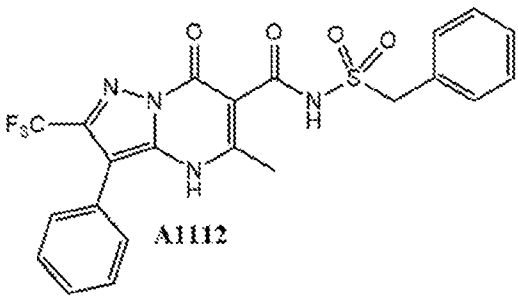
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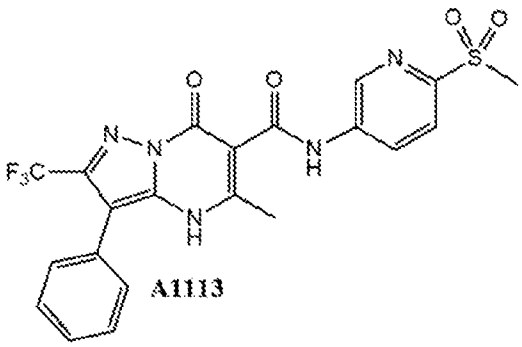
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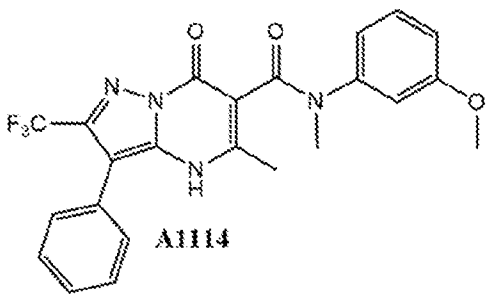
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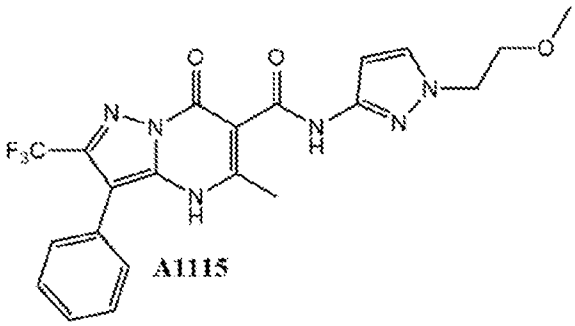
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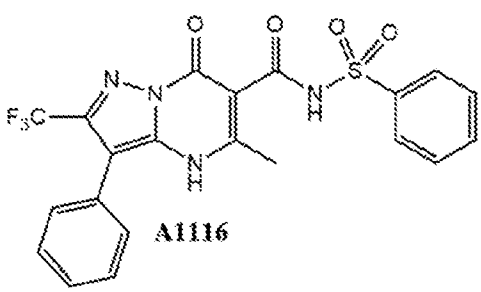
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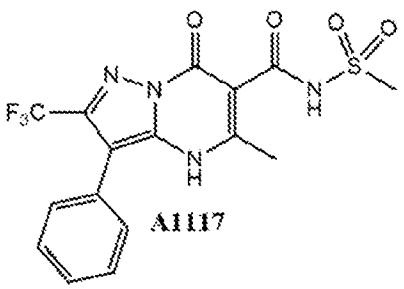
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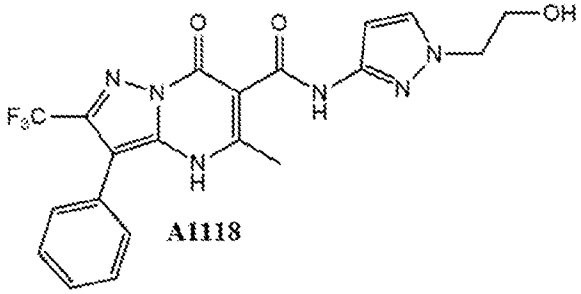
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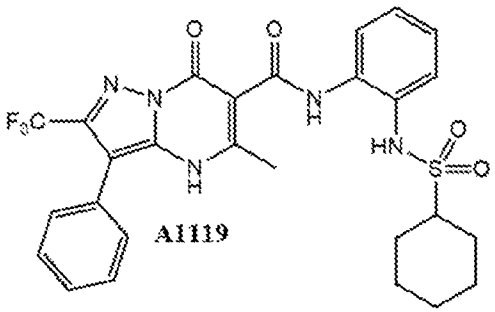
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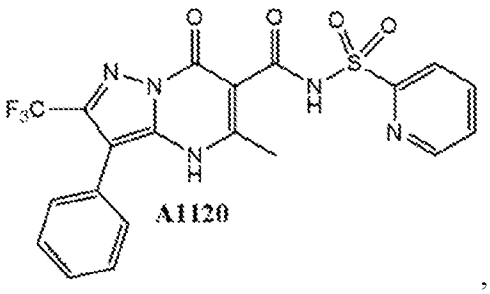
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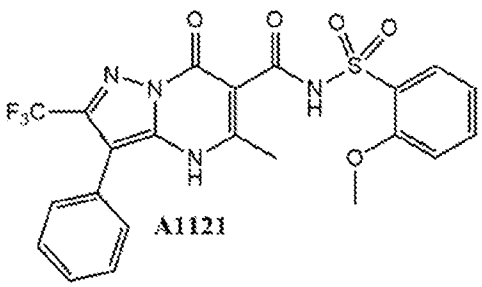
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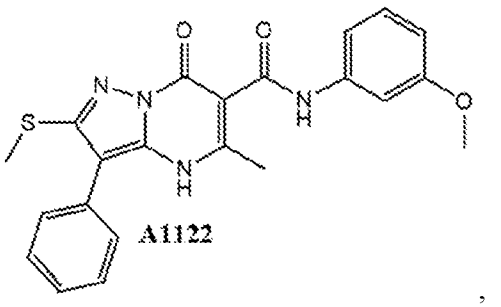
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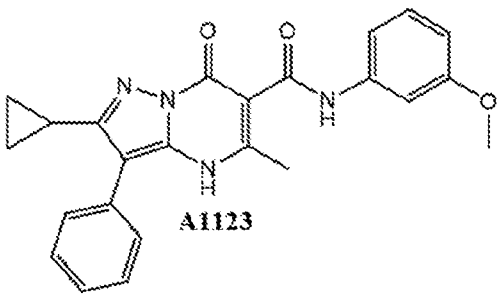
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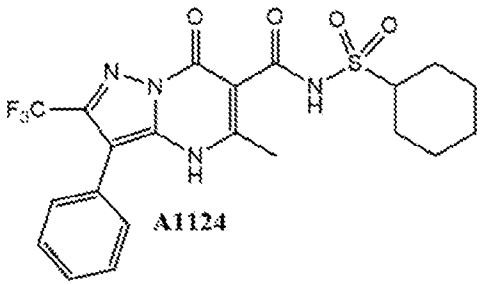
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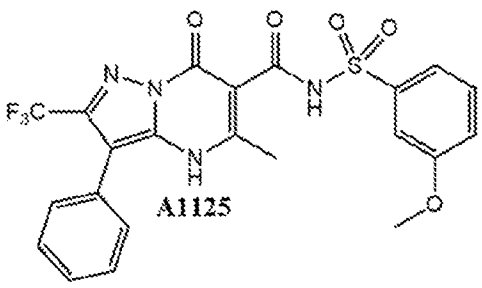
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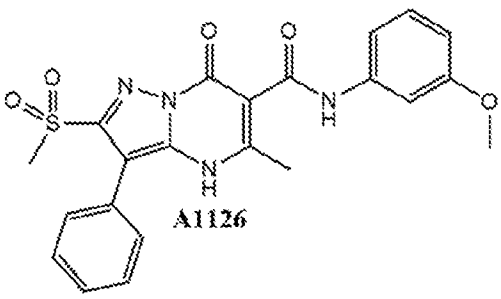
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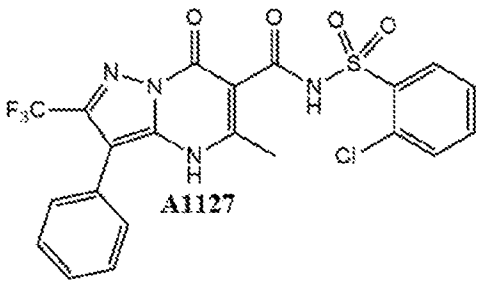
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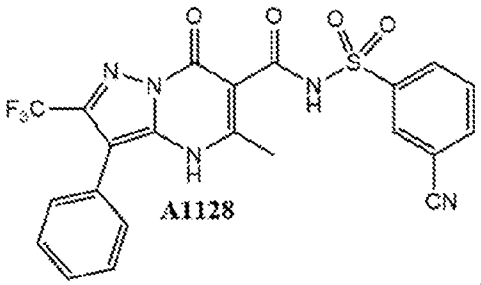


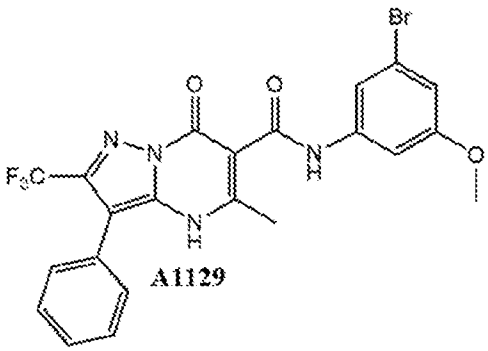
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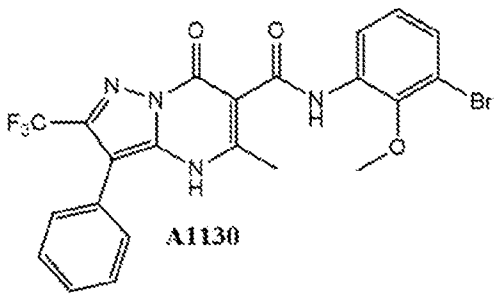


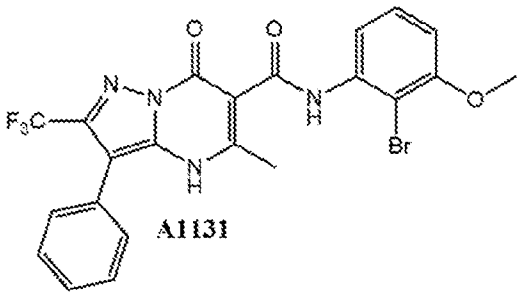
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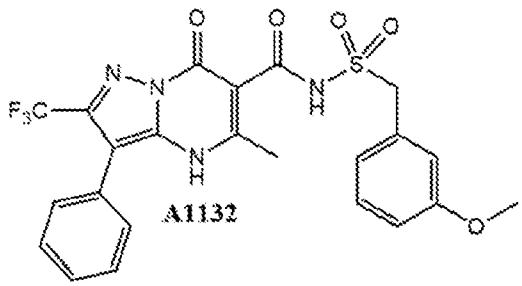

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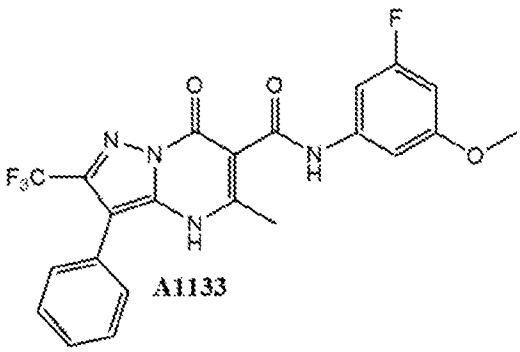

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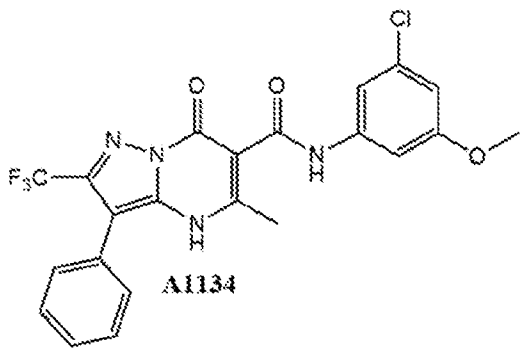

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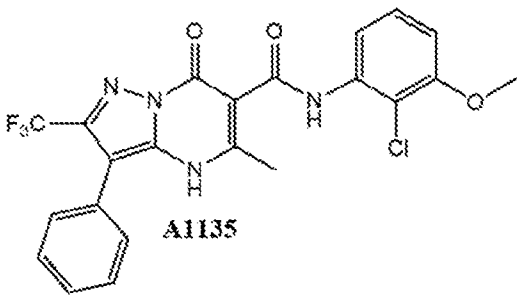

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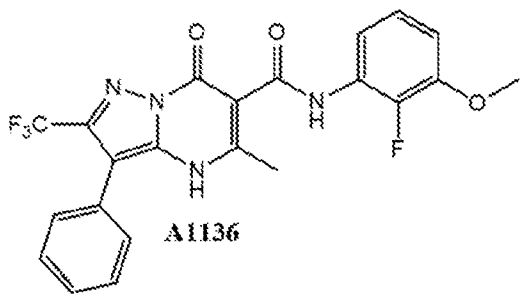

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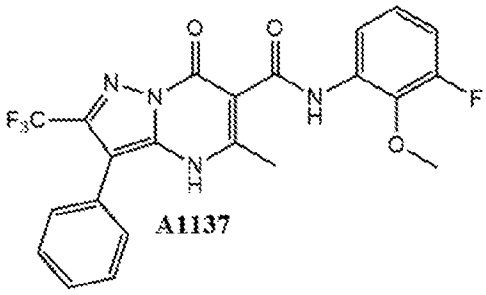

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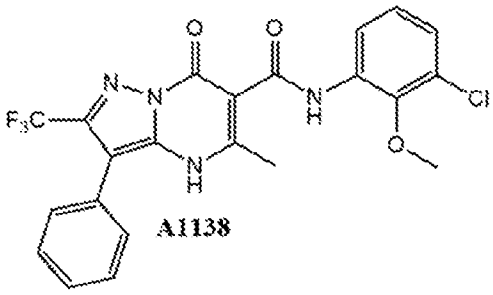

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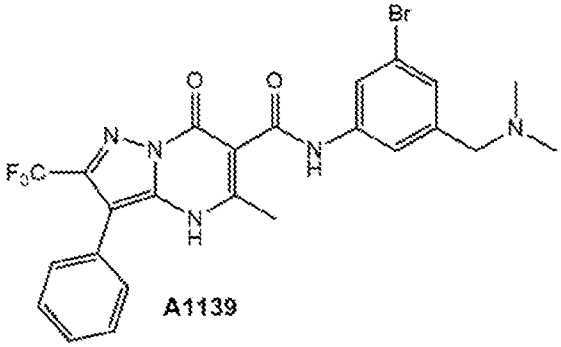

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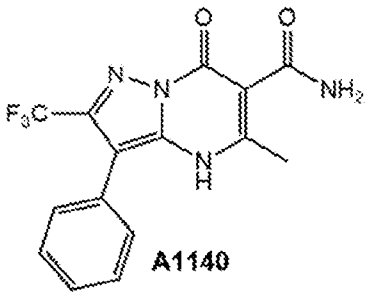

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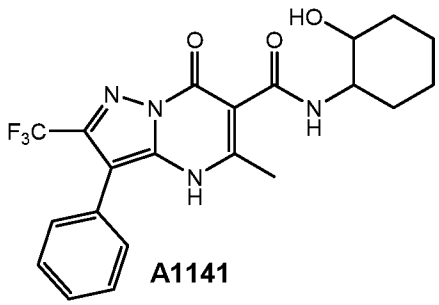

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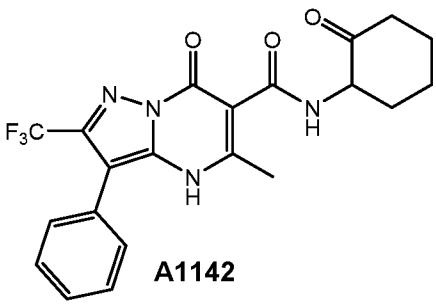

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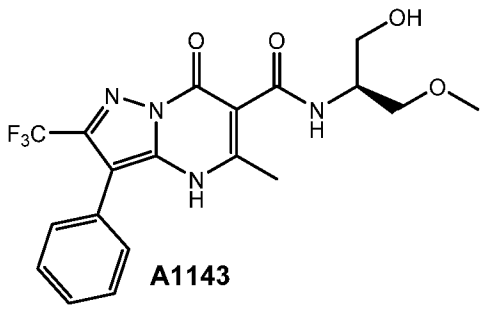

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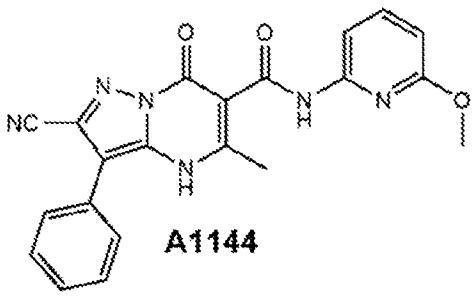

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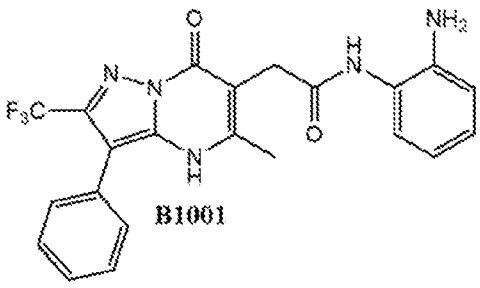

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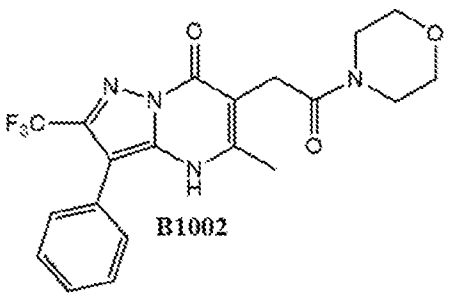

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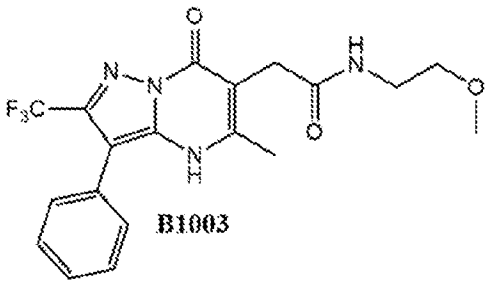

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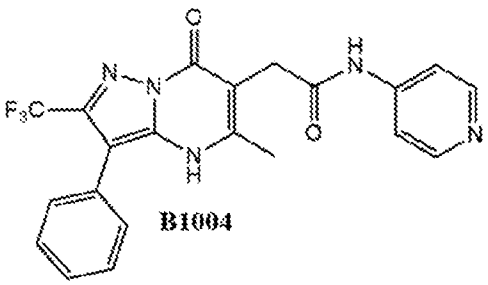

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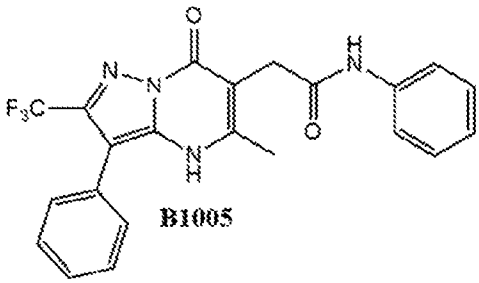

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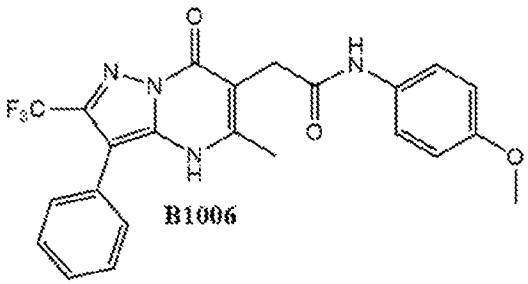
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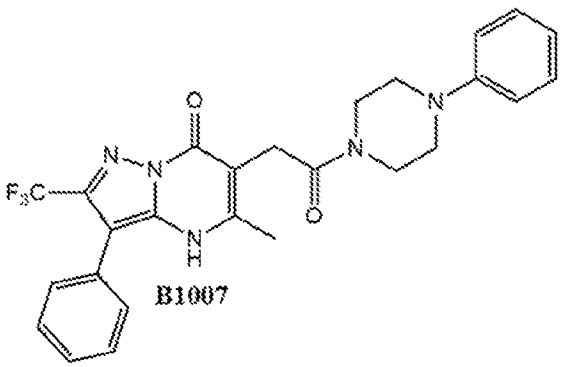
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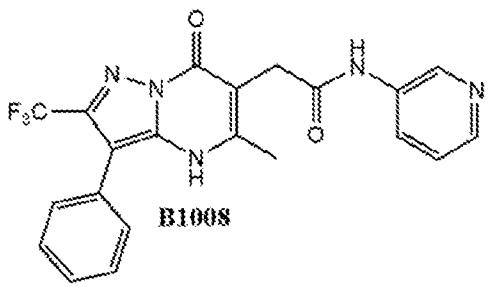
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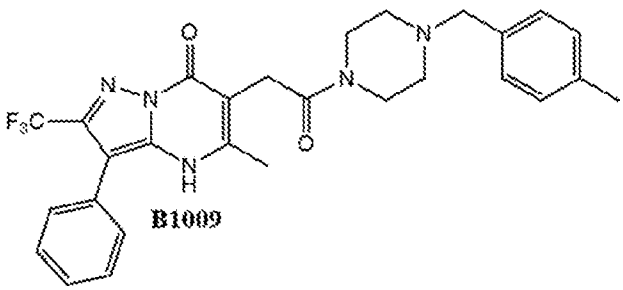
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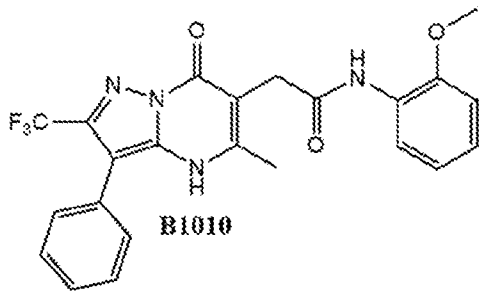
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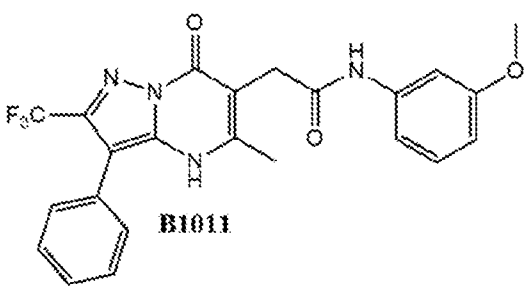
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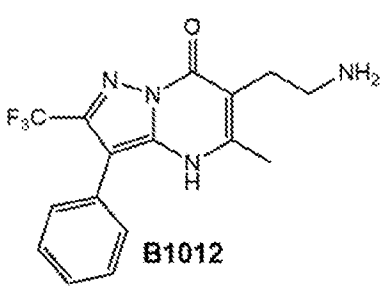
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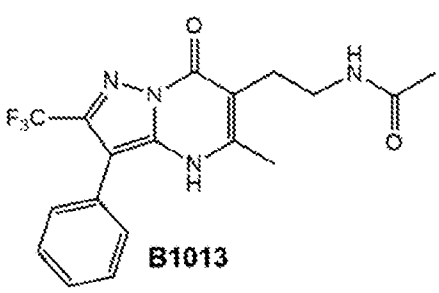
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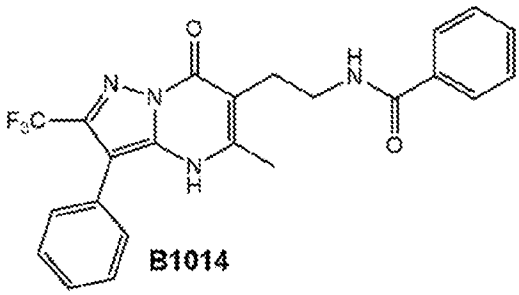
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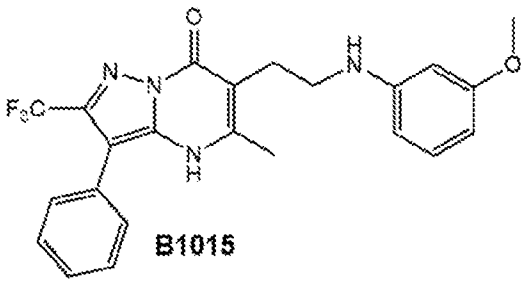
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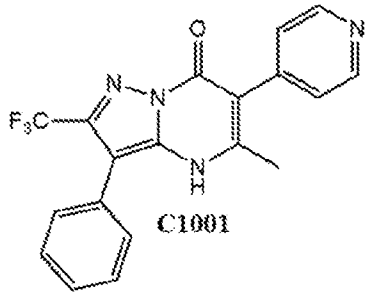
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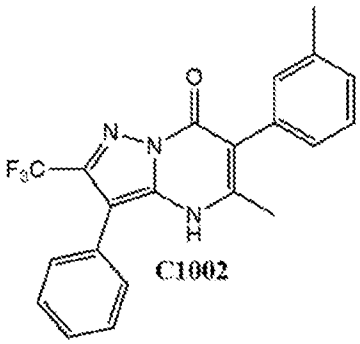
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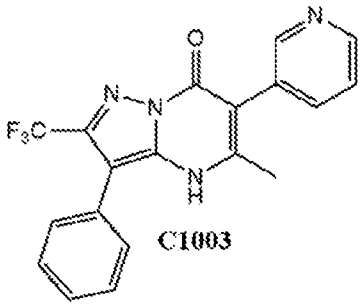
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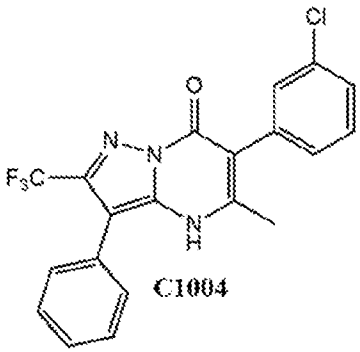
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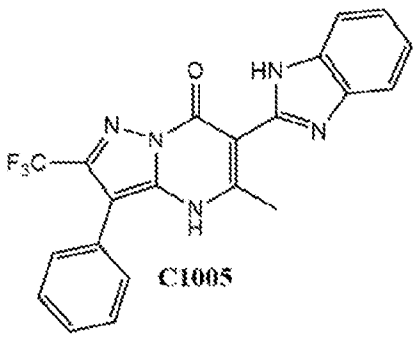
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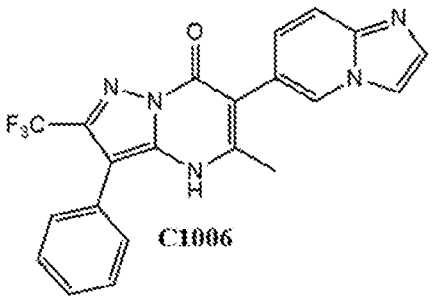
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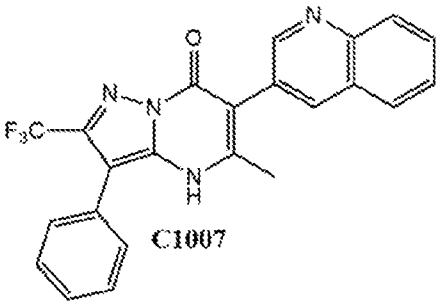
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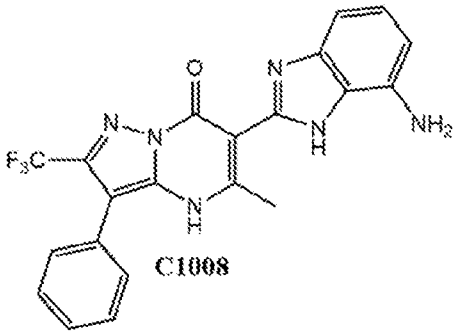
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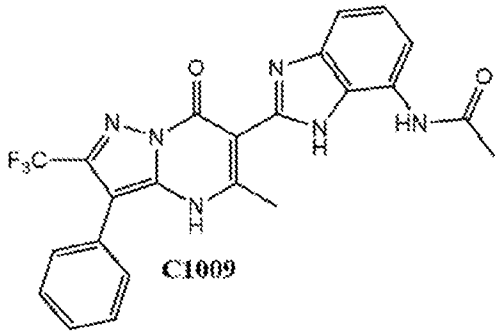
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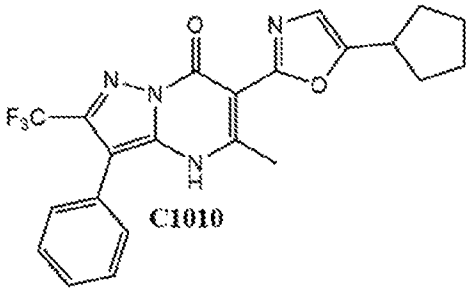
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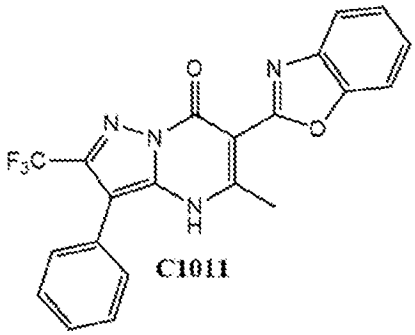
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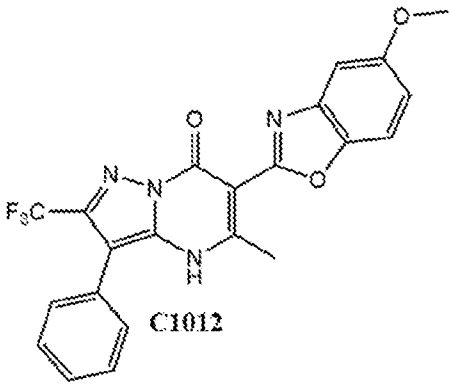
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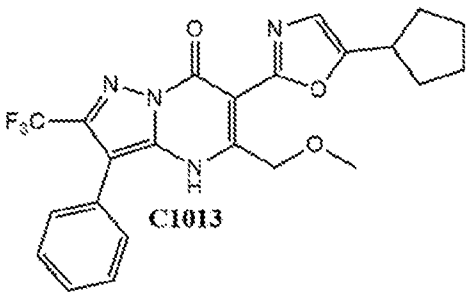
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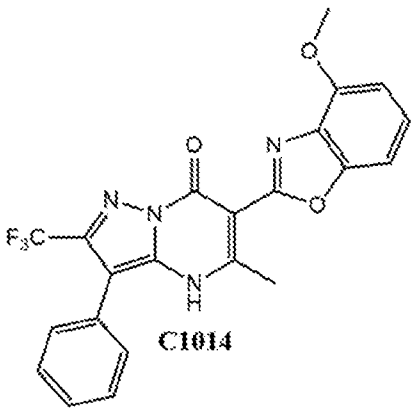
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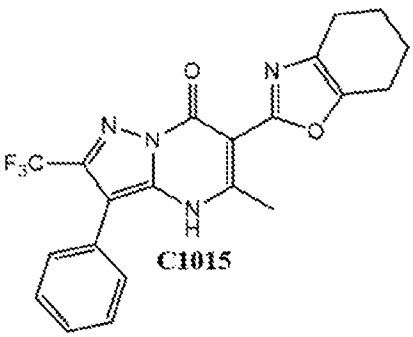
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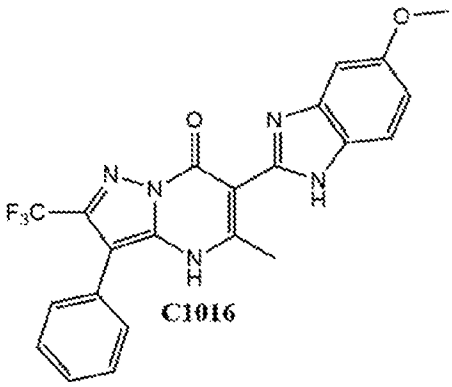
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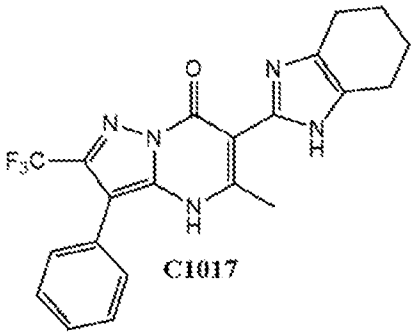
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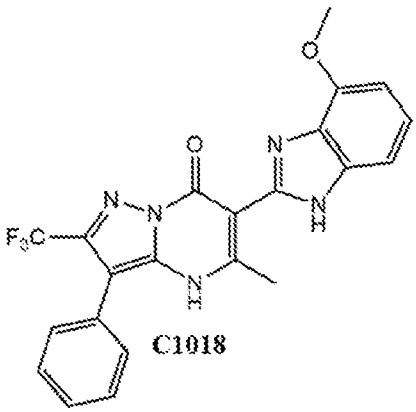
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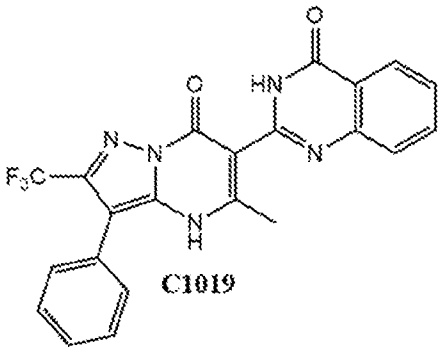
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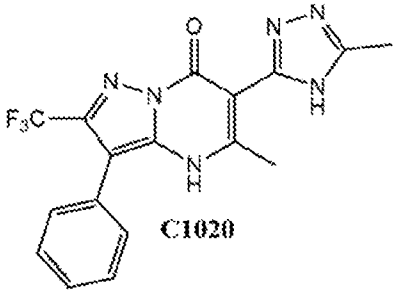
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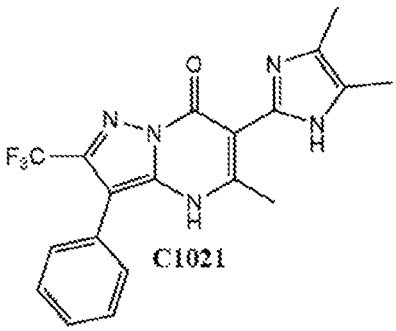
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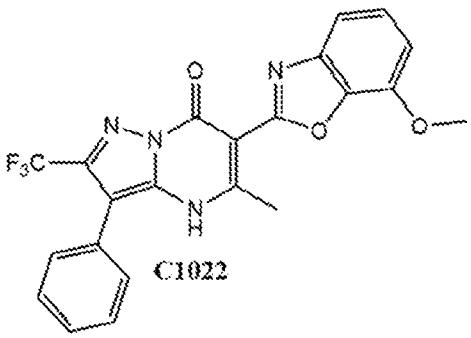
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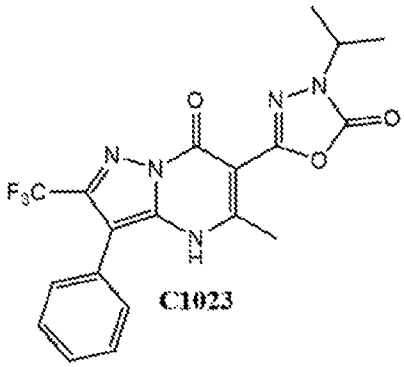
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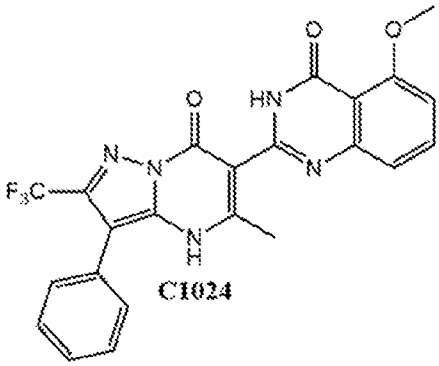
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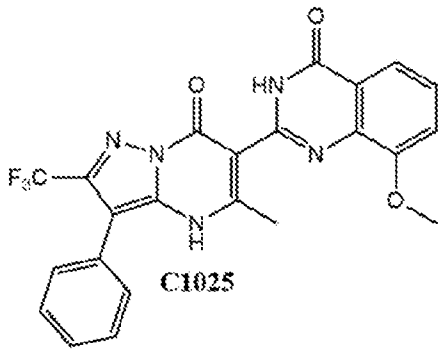
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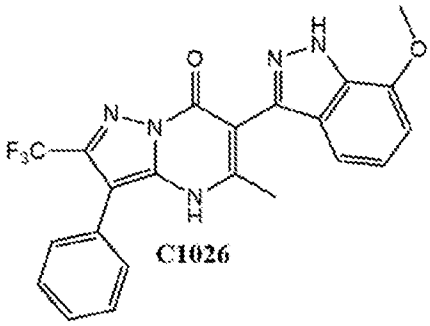
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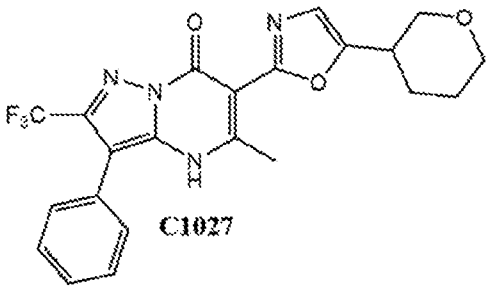
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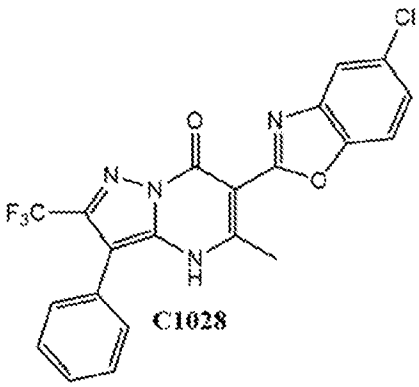
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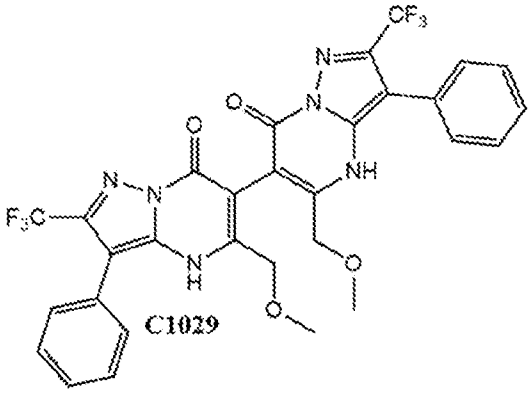
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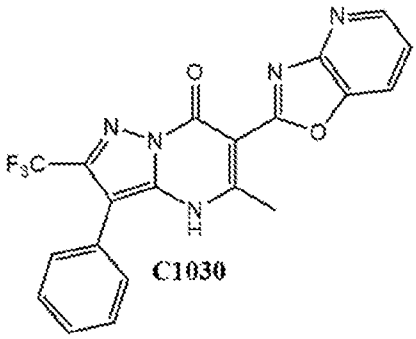
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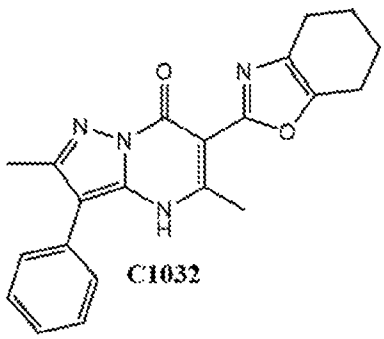
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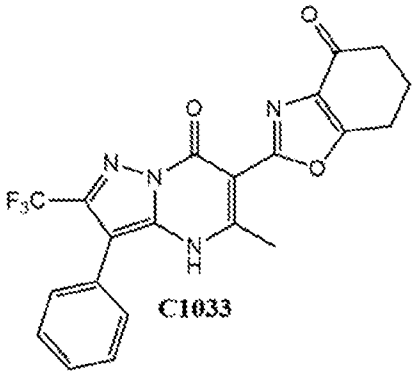
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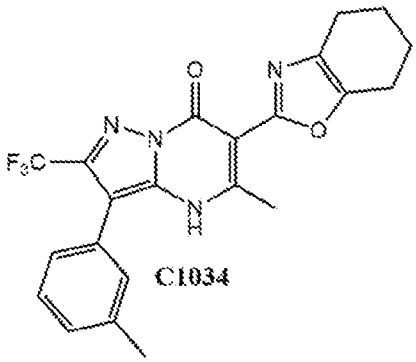


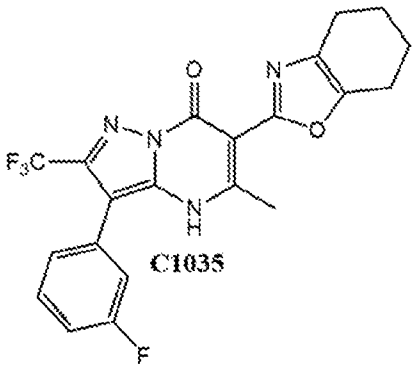
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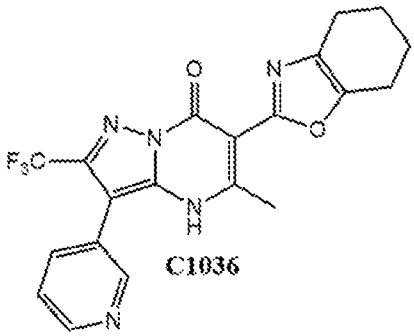


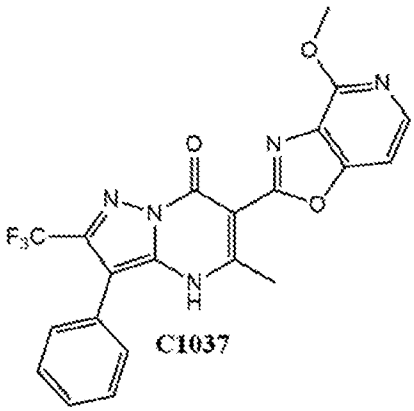
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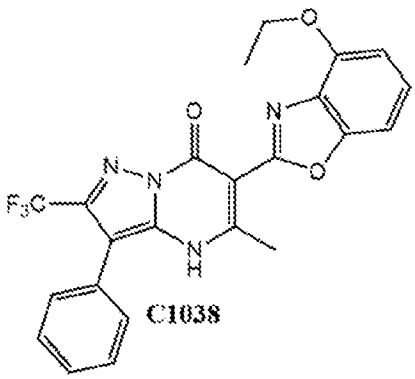

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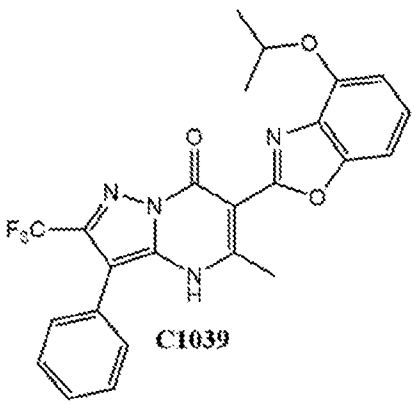

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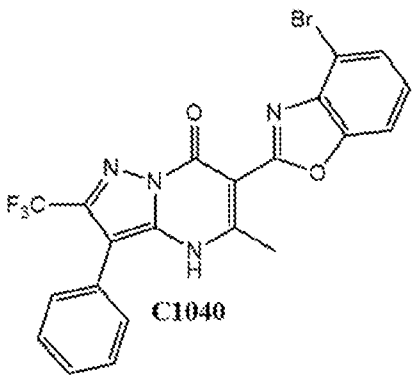

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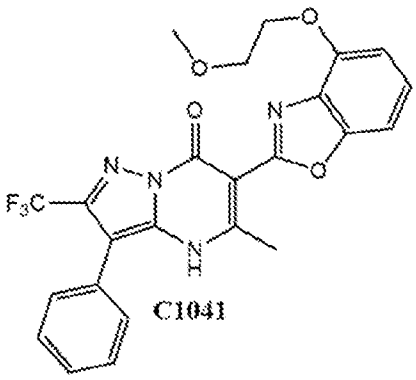

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C1037

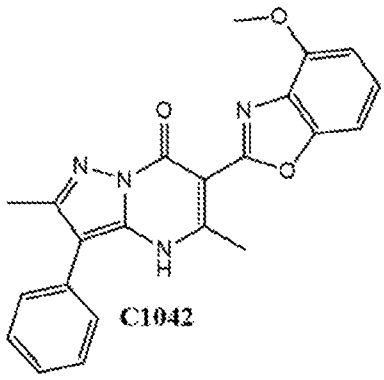

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C1039

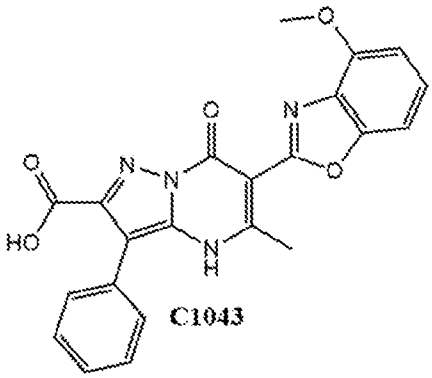

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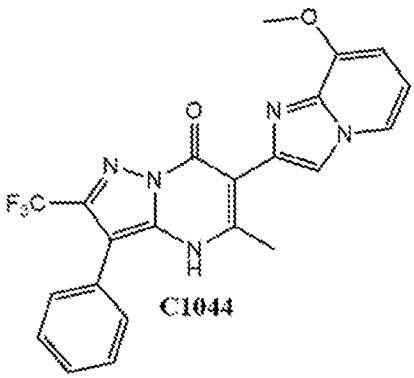
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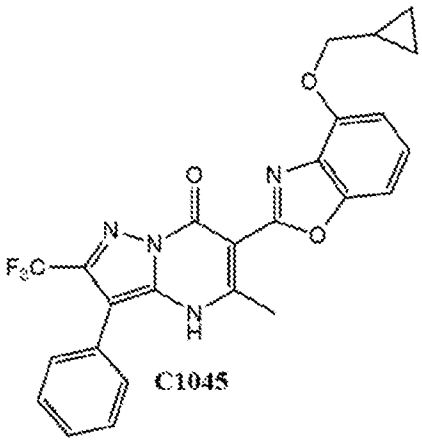
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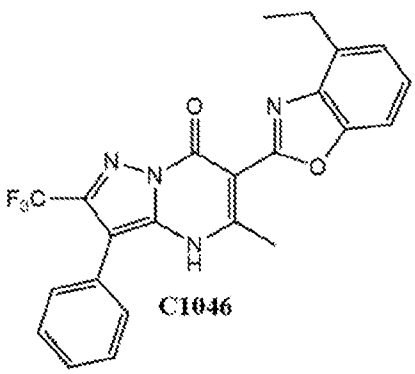
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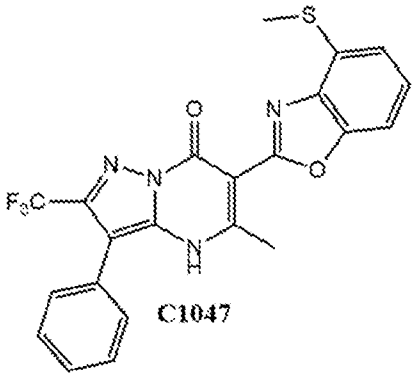
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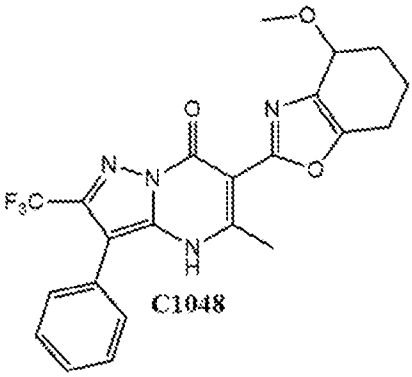
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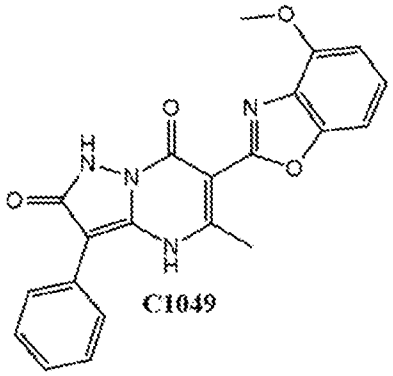
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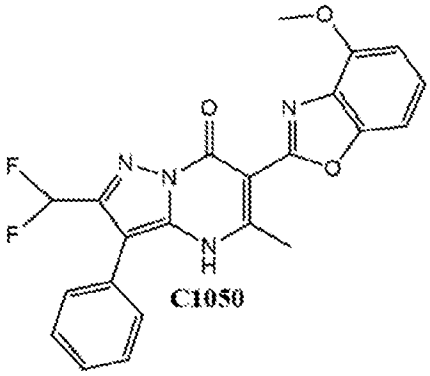
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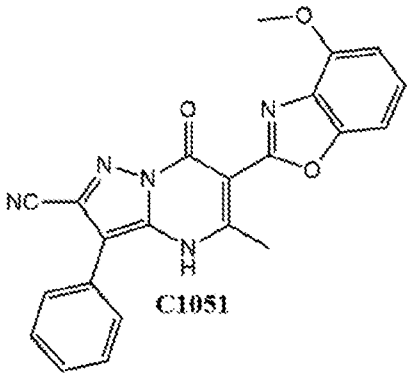
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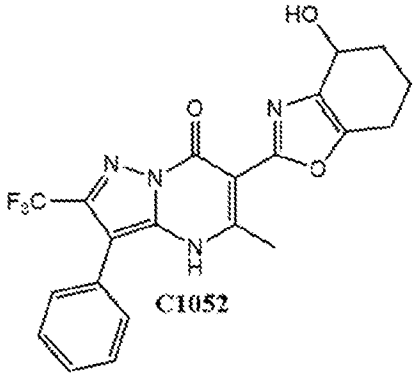
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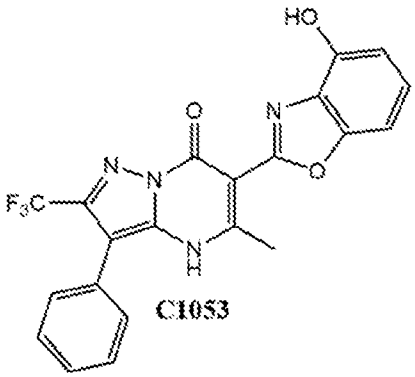
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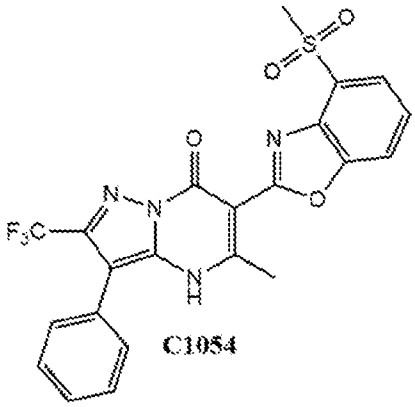
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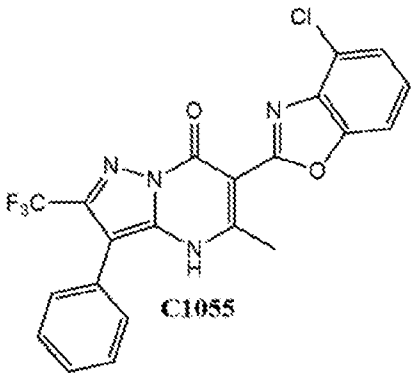
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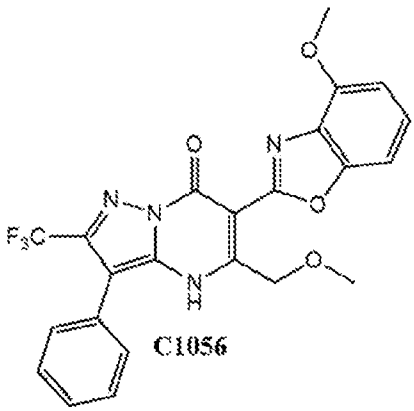
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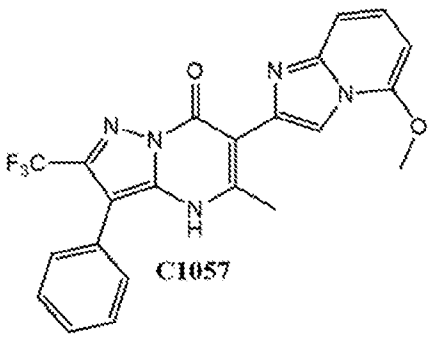
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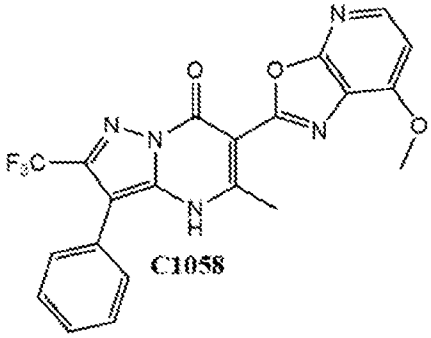
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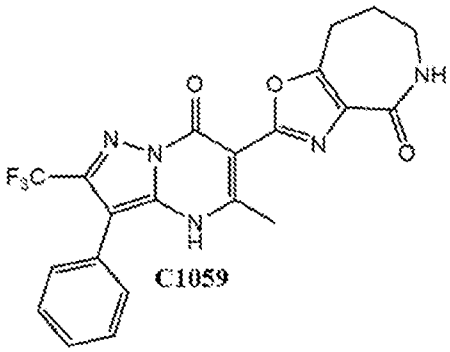
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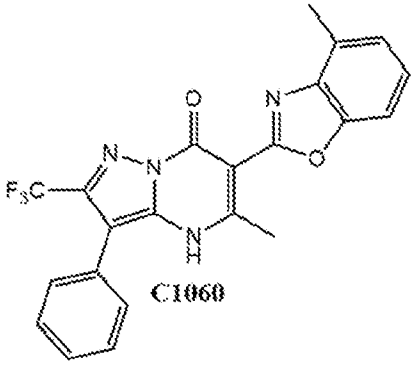
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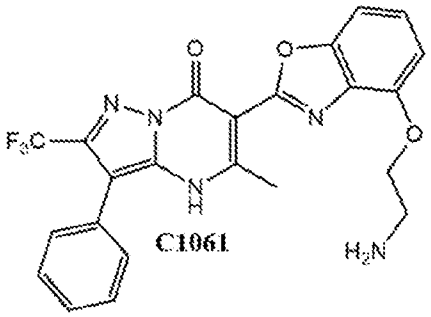
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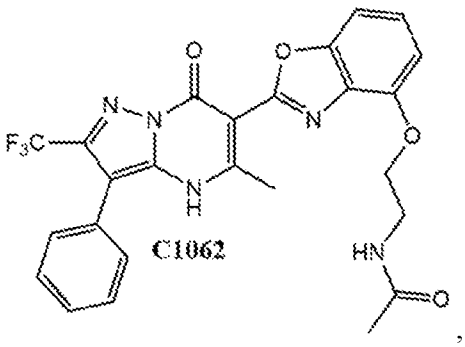
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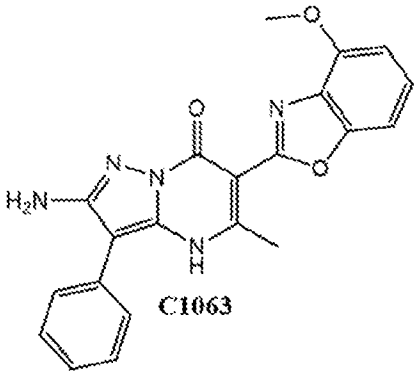
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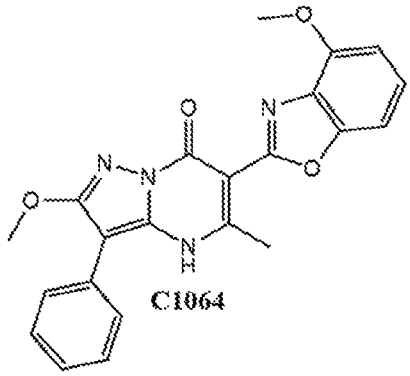
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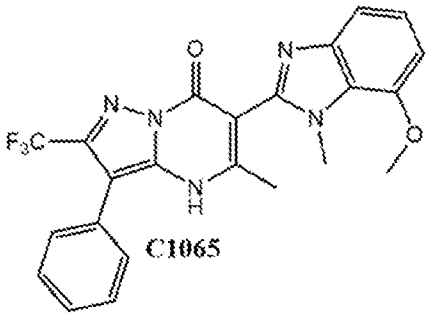
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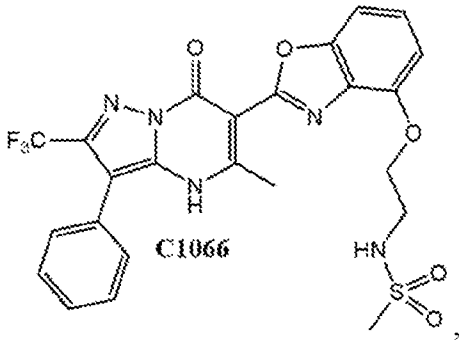


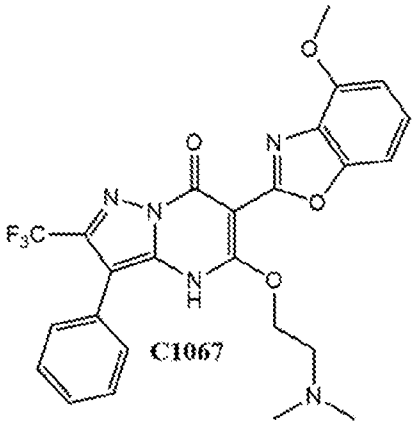
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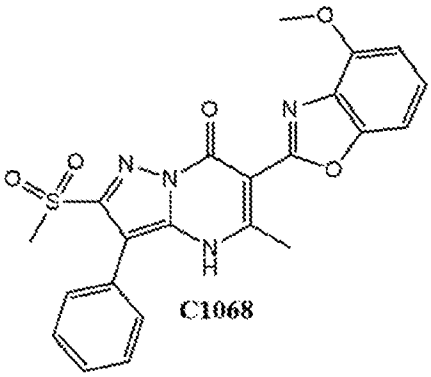


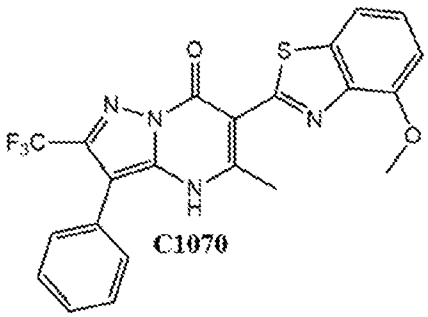
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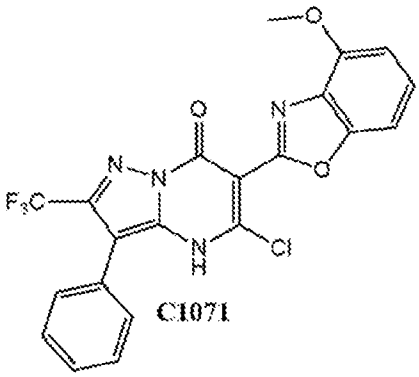

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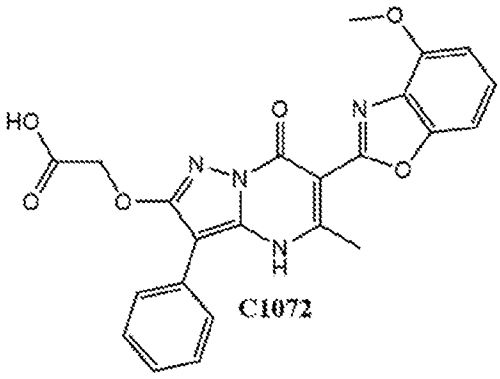

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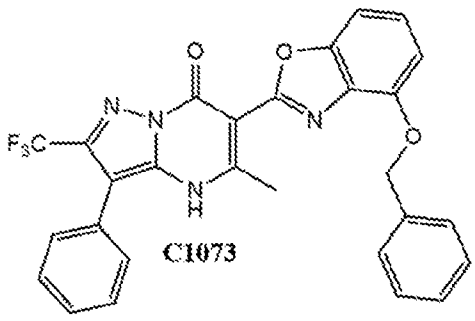

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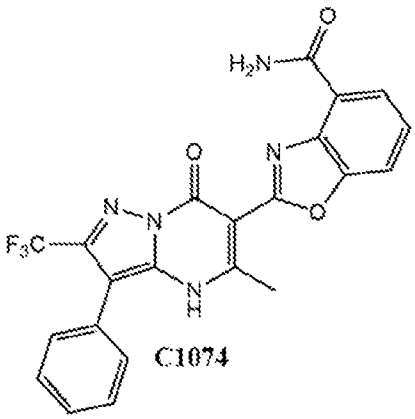

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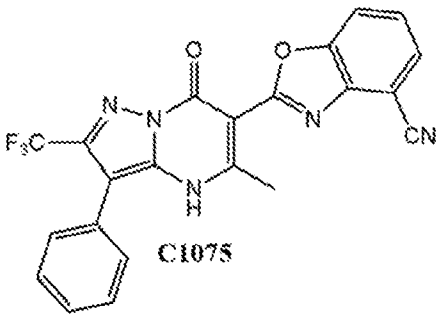

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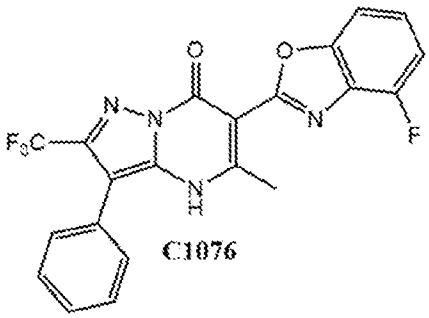

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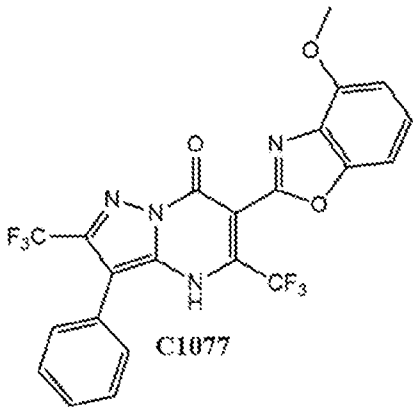
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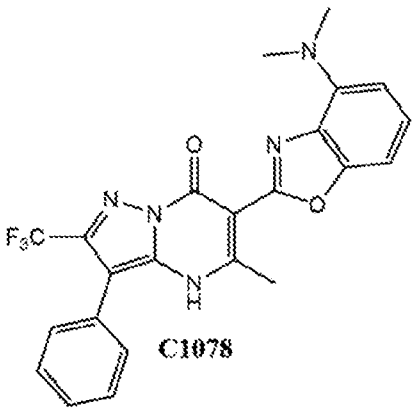
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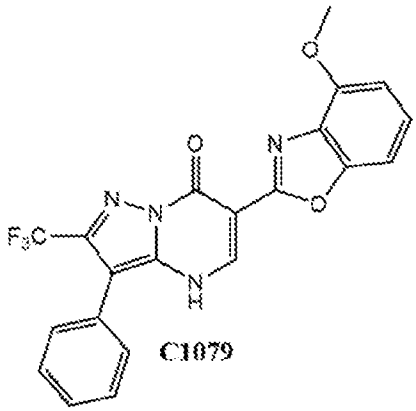
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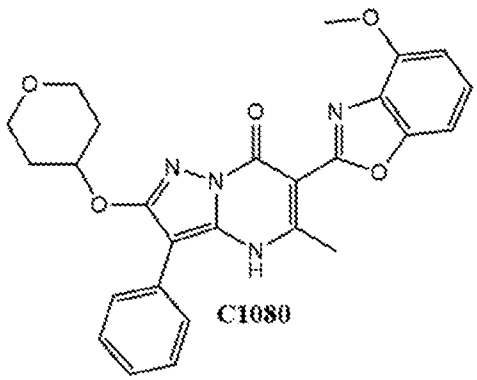
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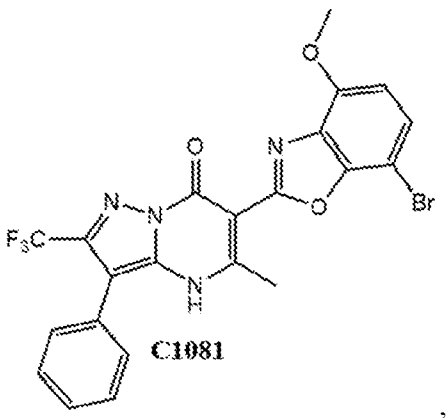
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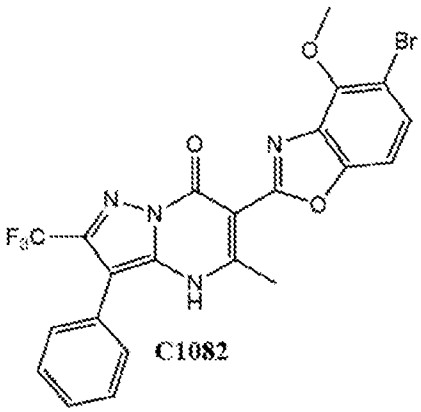
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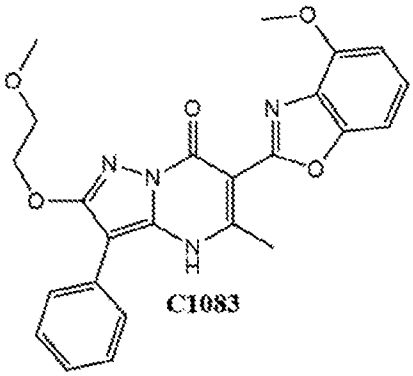
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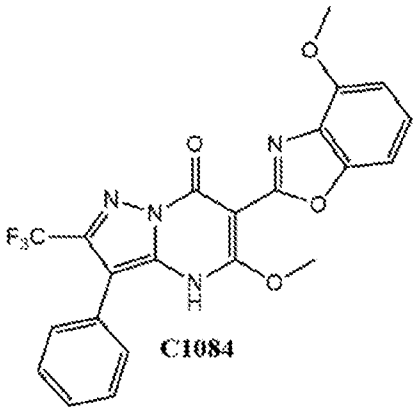
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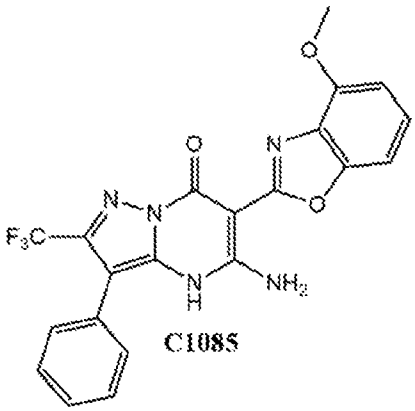
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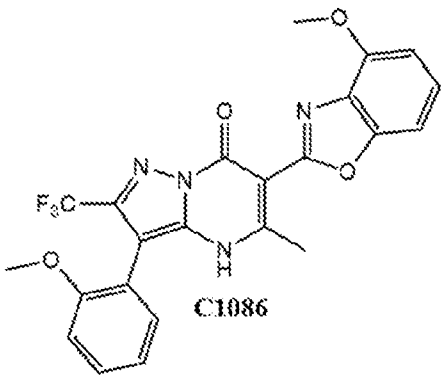
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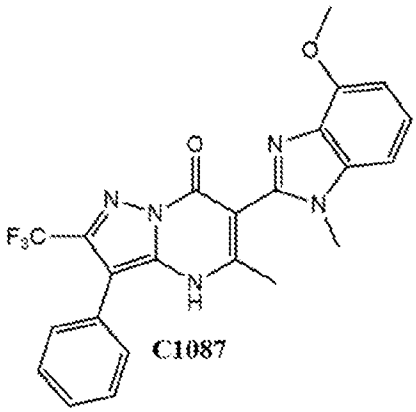
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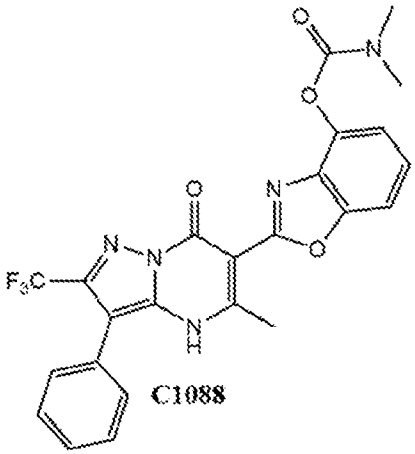
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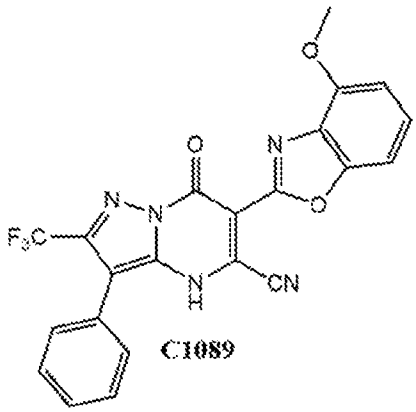
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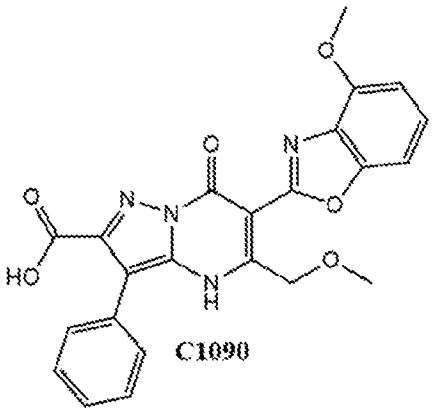
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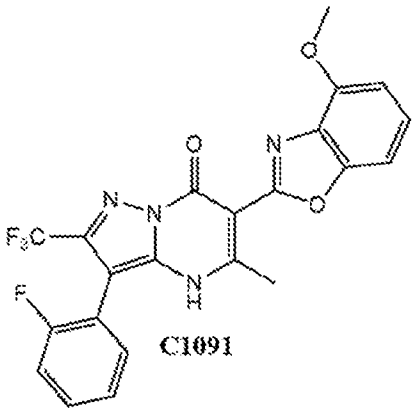
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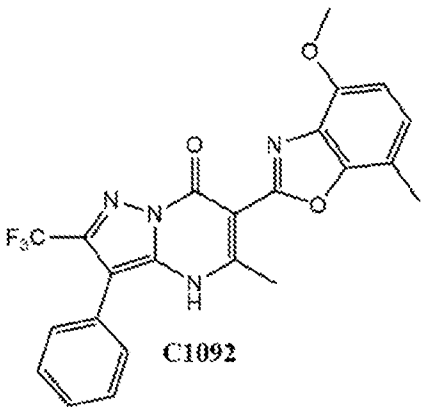
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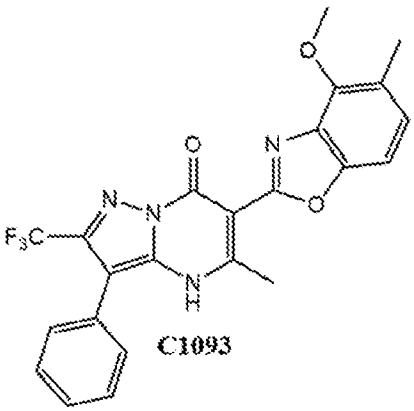
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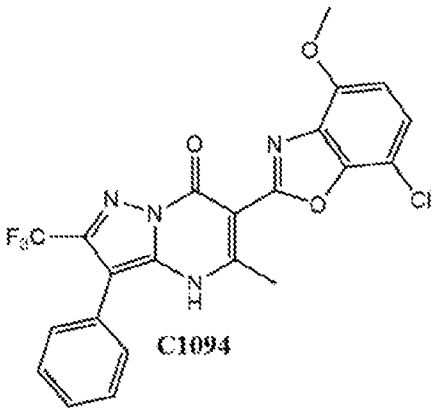
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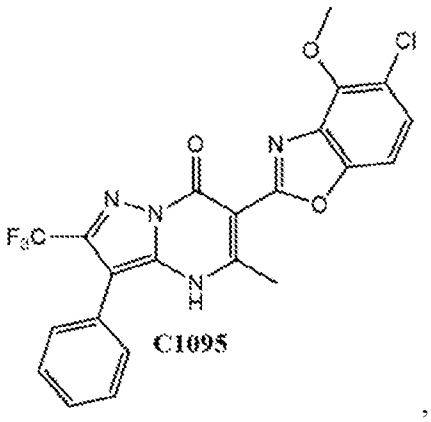
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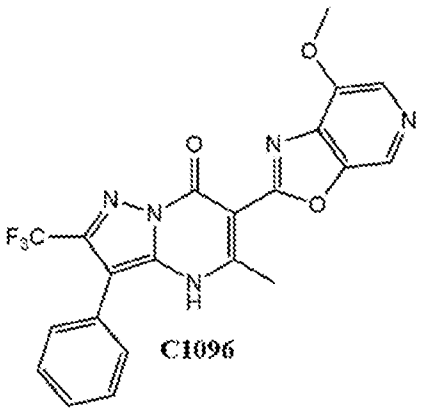
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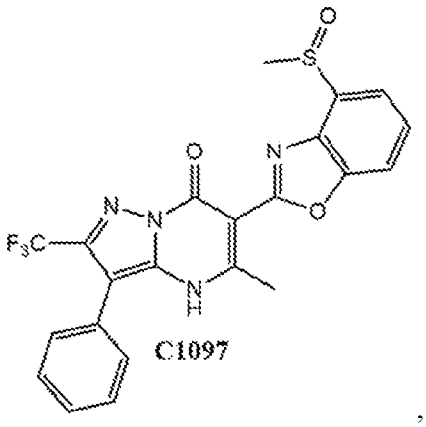
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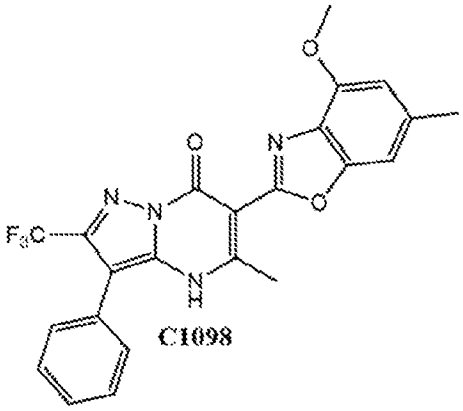
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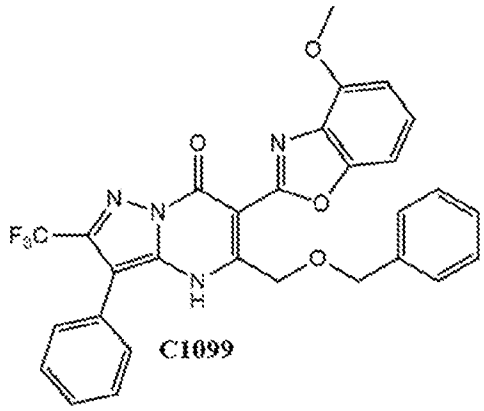
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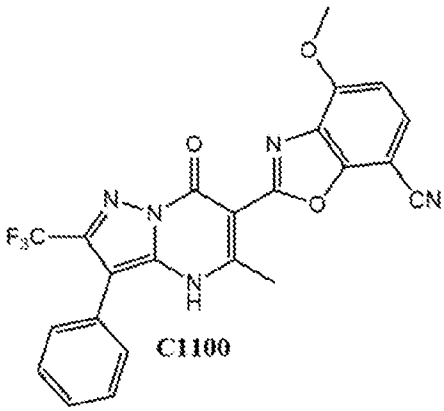
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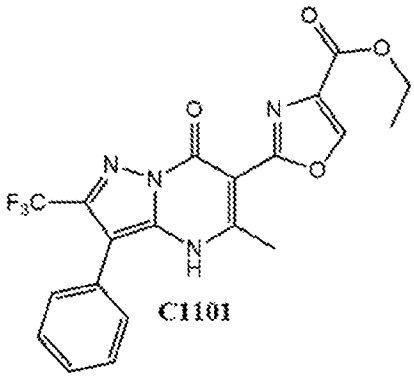
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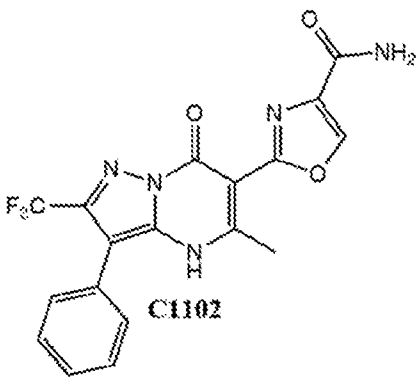
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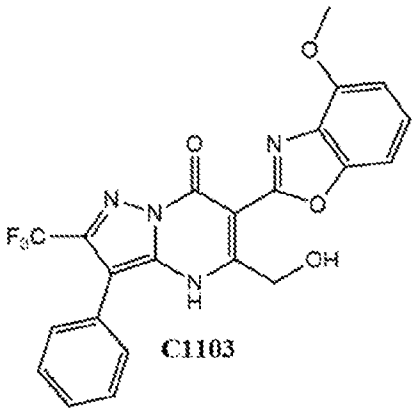
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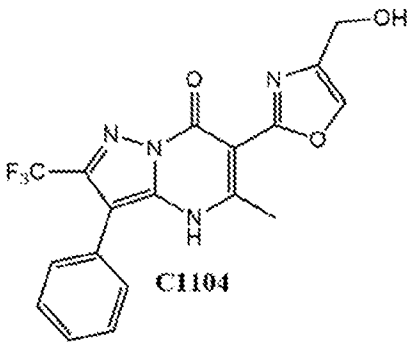
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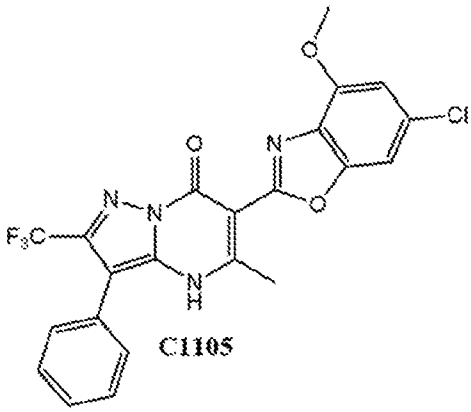
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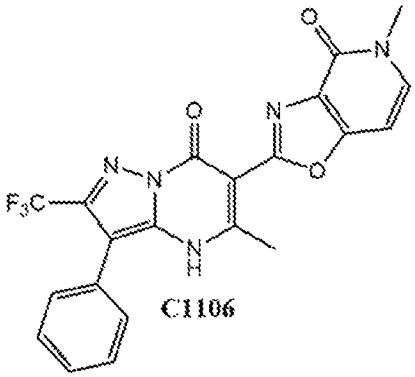
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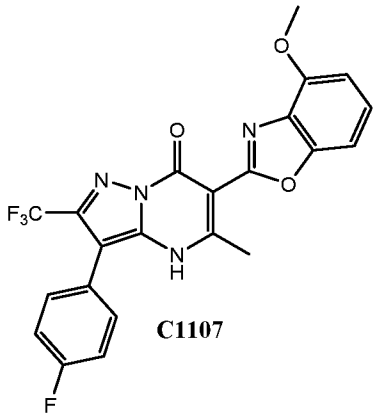
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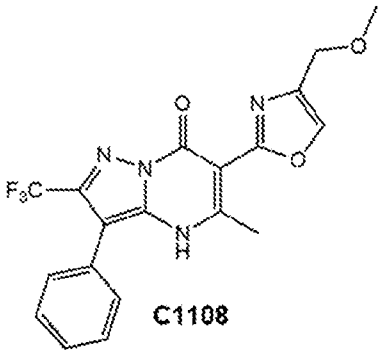
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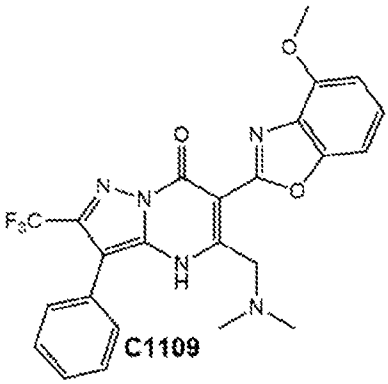
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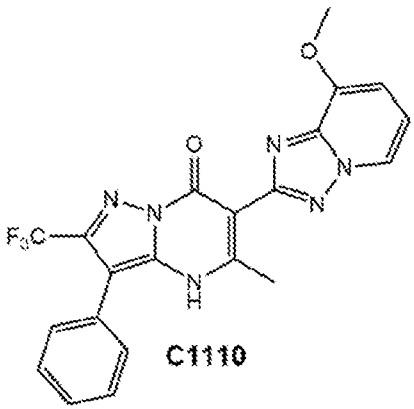
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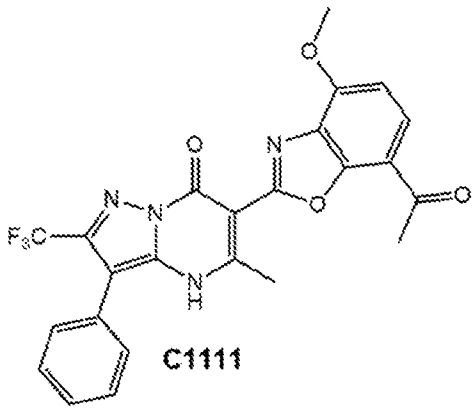
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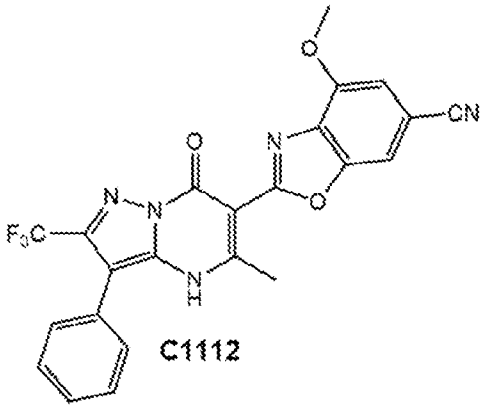
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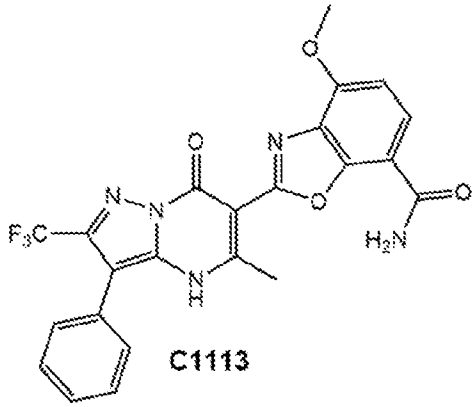
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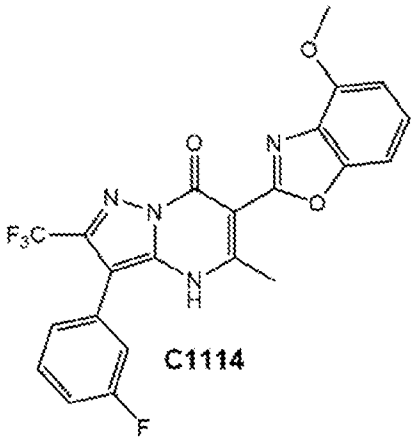
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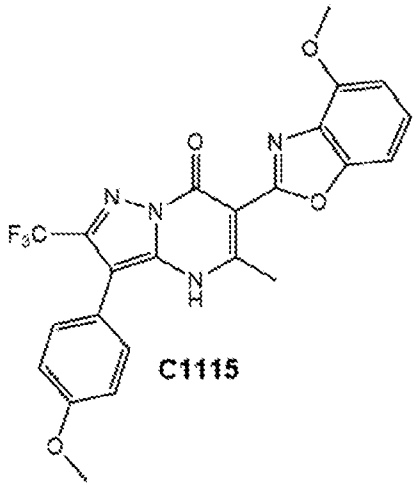
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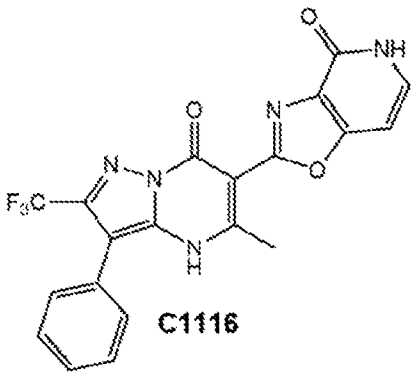
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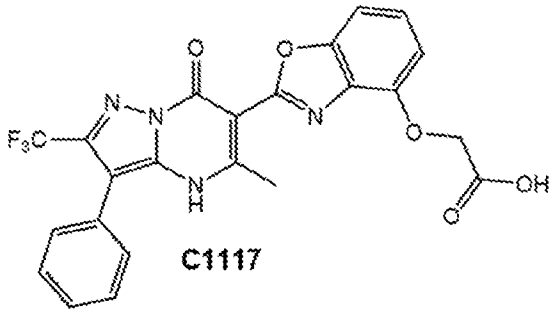
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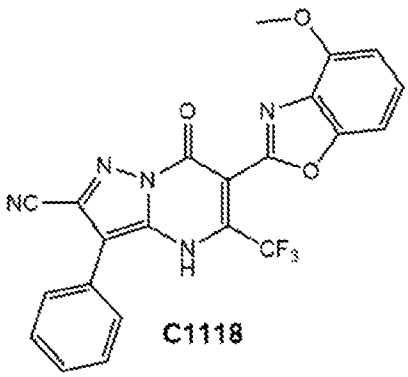
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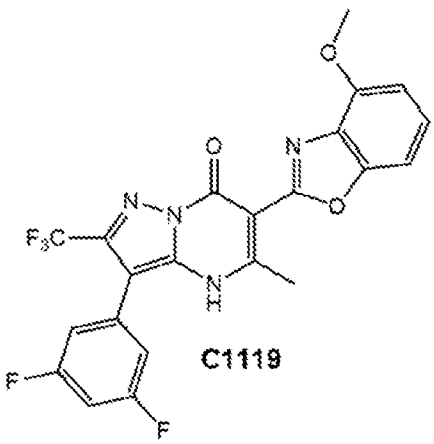
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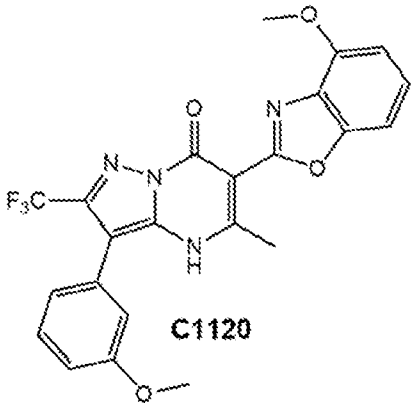
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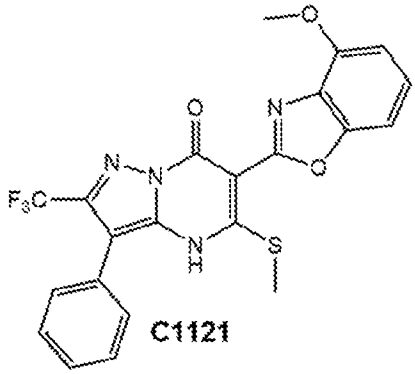
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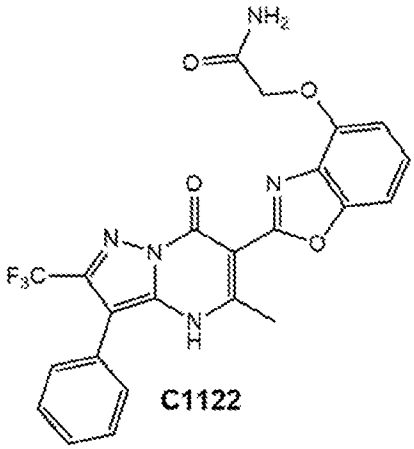
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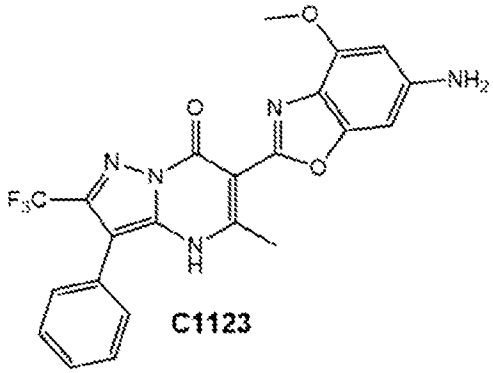
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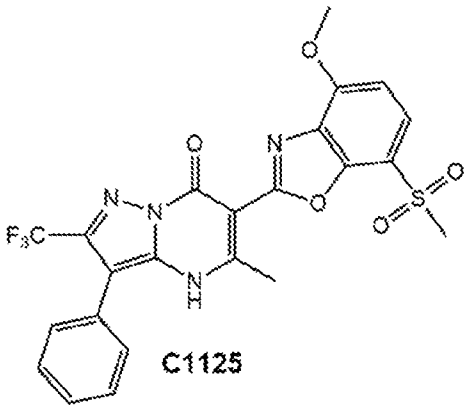
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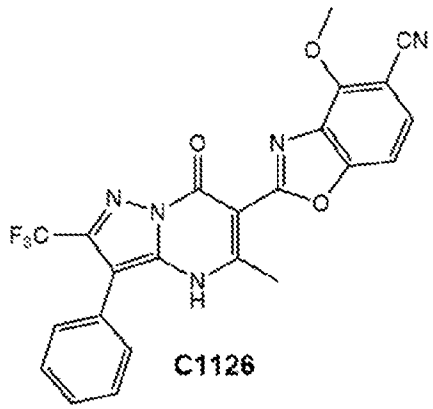
C1122



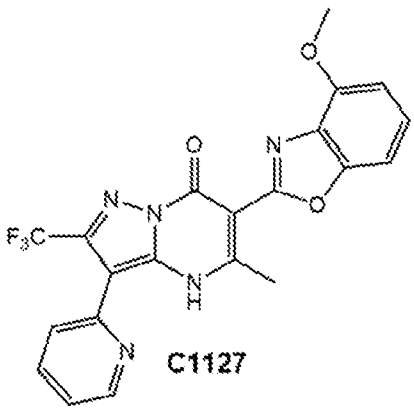
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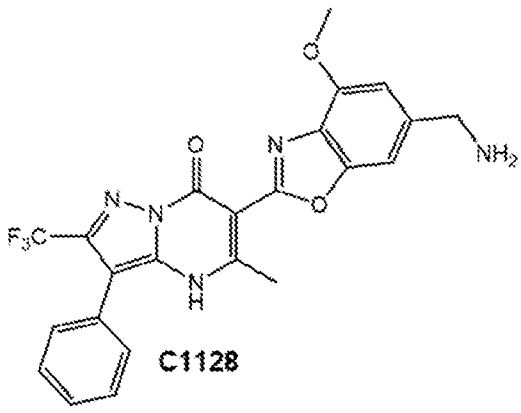
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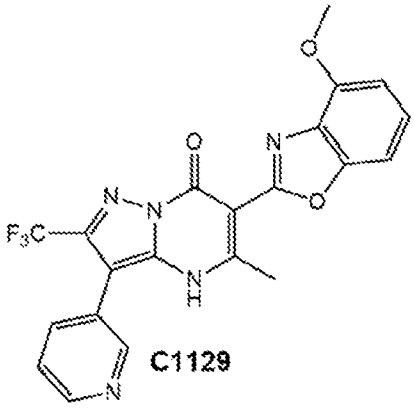
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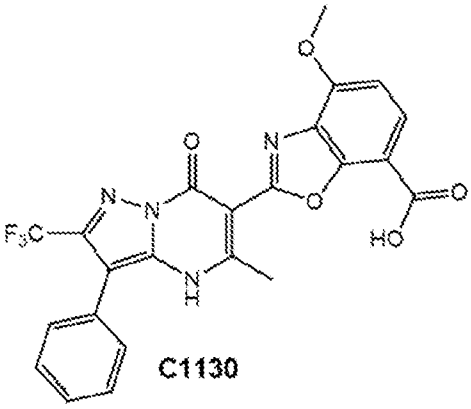


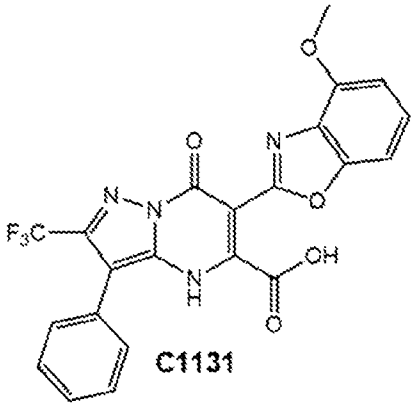
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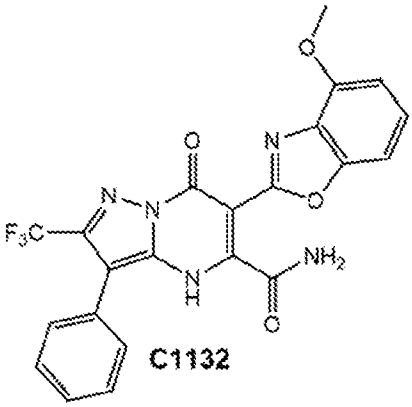


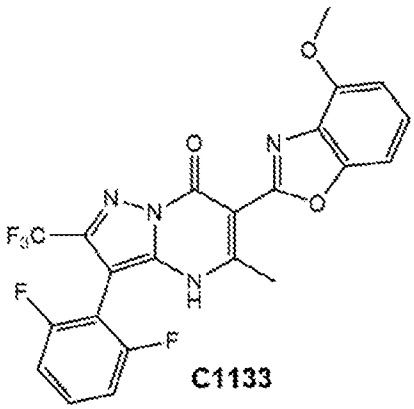
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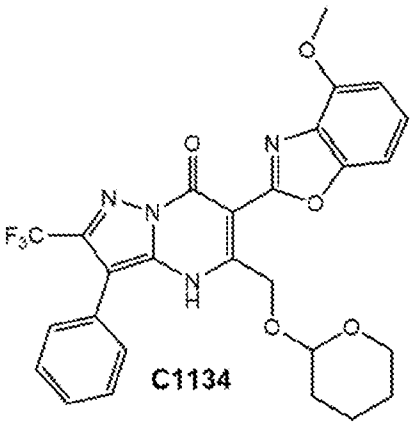

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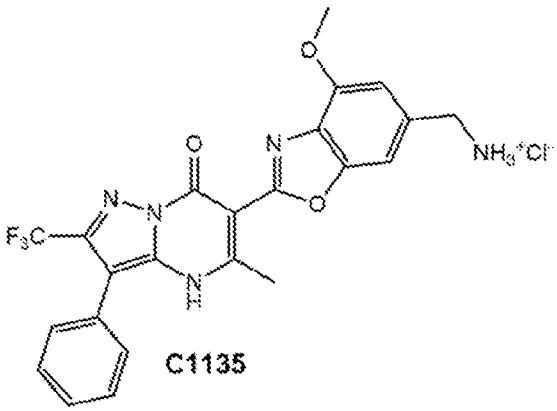

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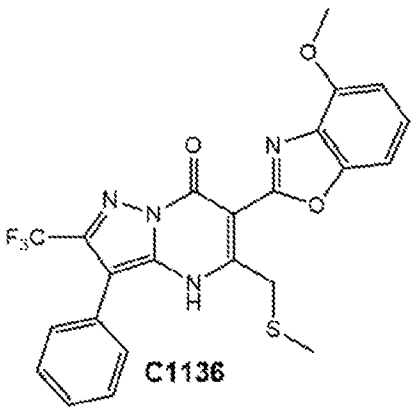

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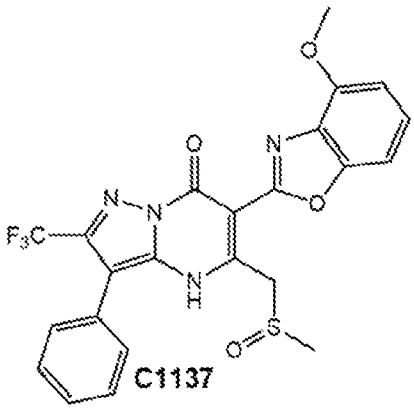

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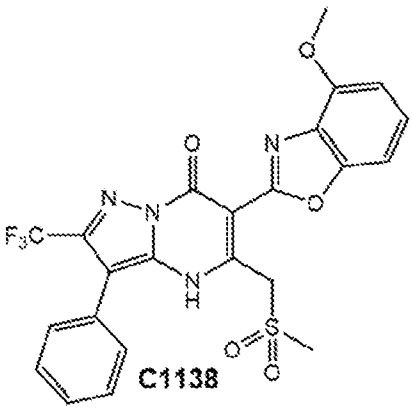

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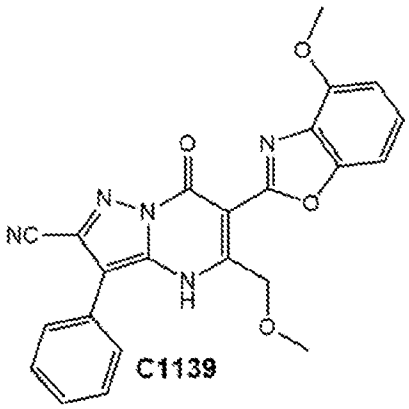

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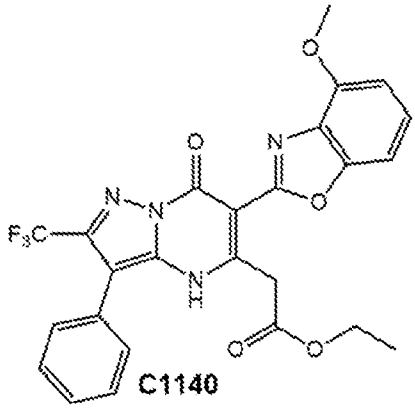

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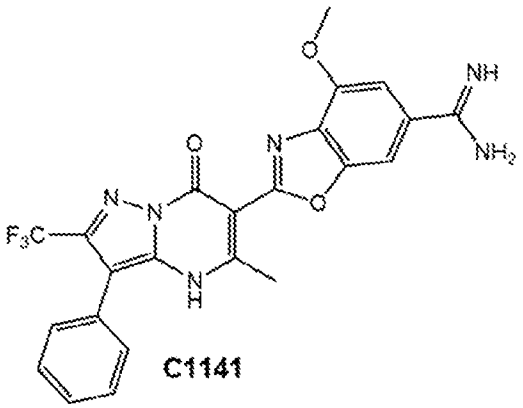

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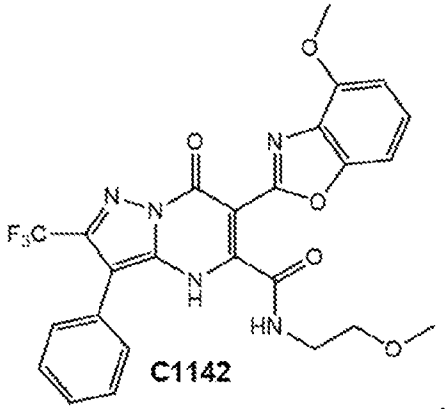

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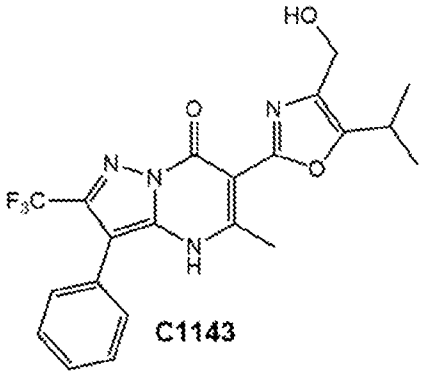

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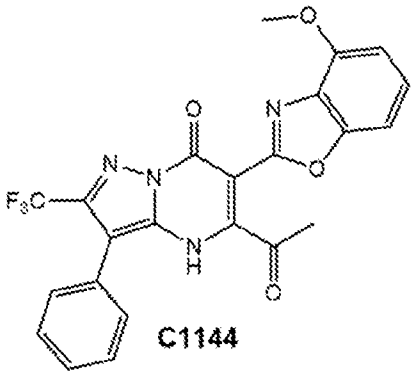

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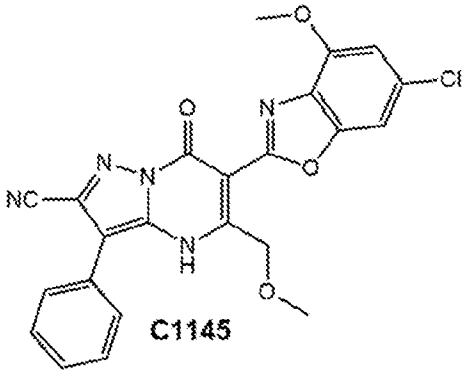

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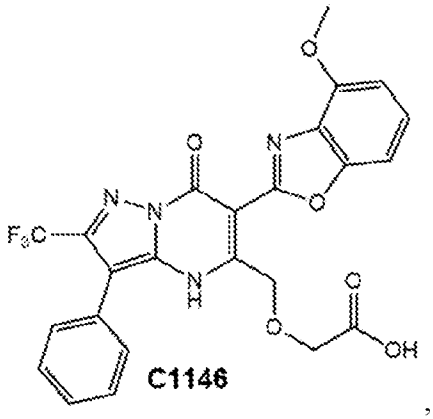

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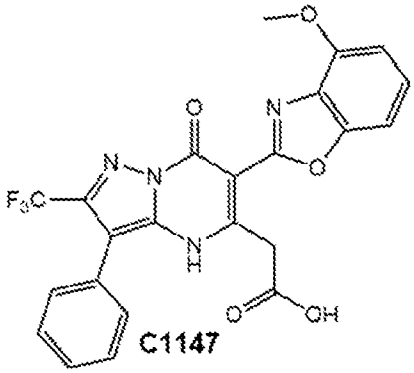

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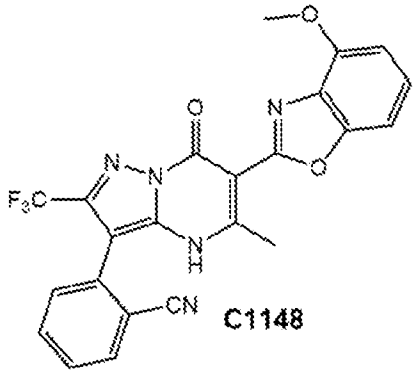
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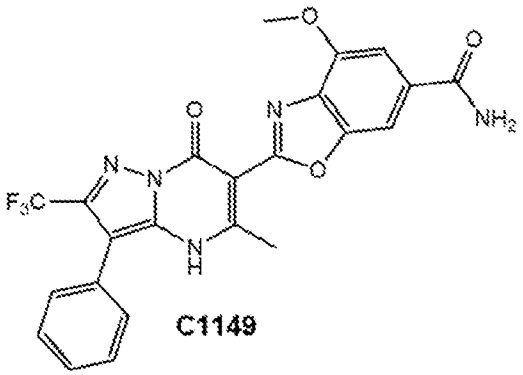
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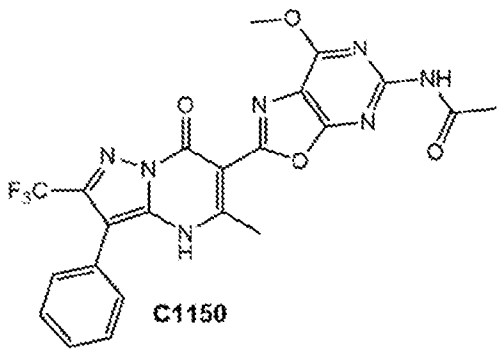
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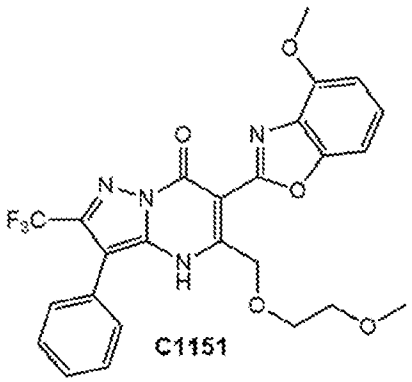
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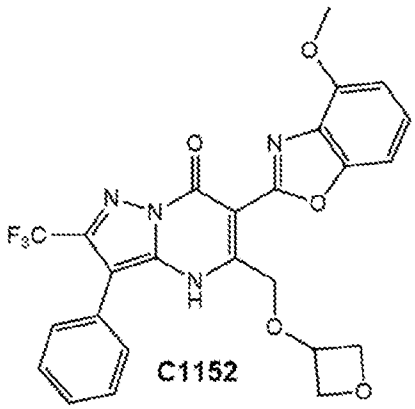
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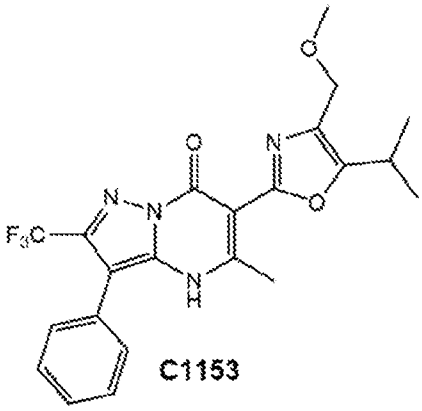
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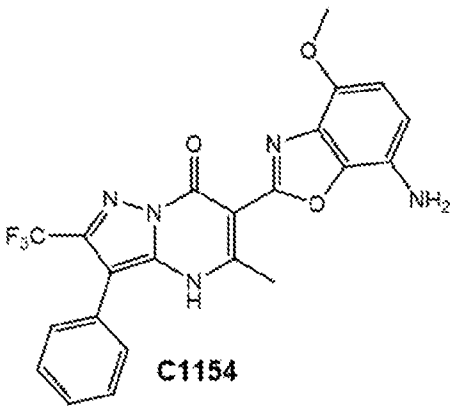
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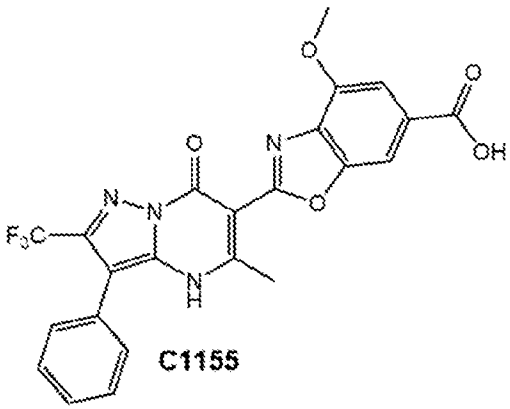
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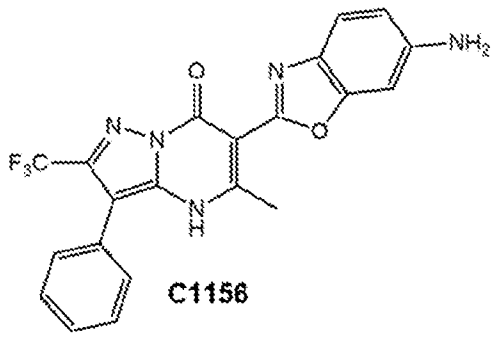
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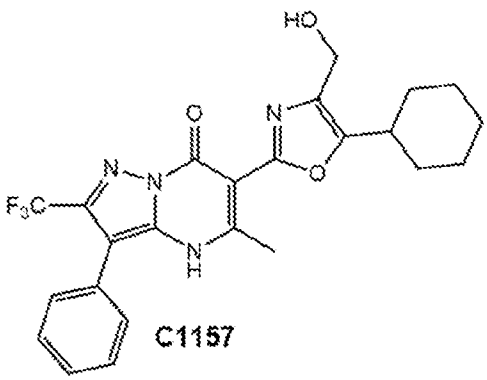
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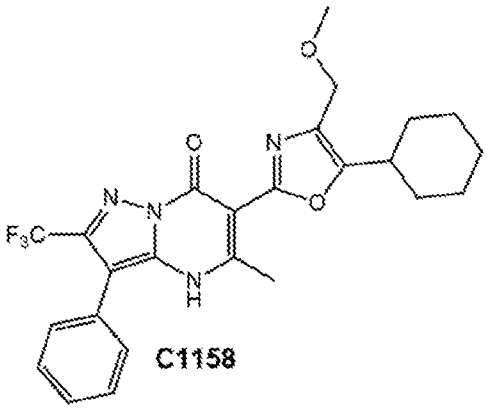
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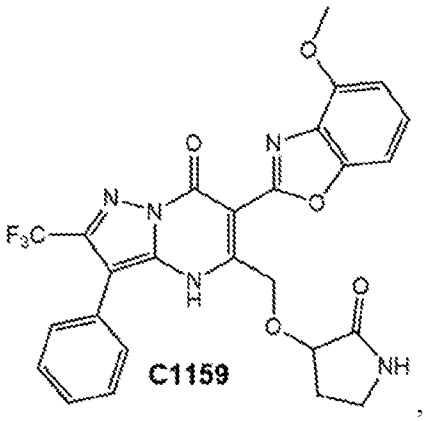
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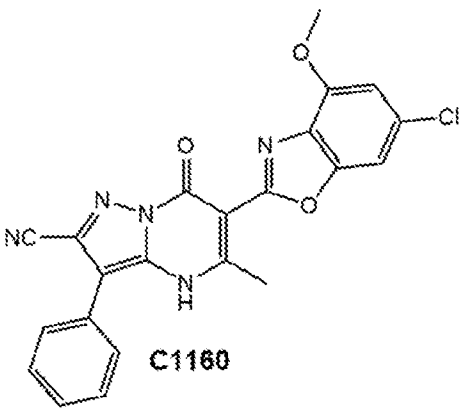
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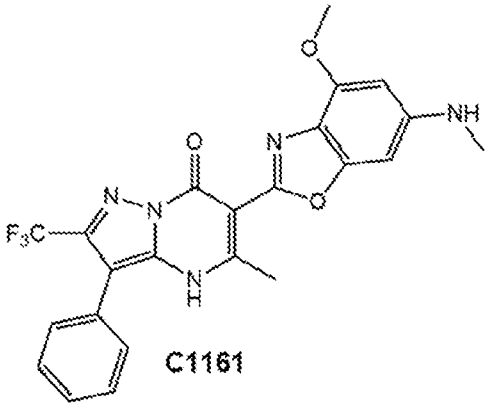
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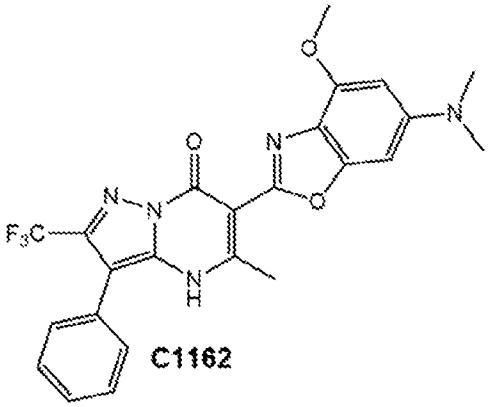
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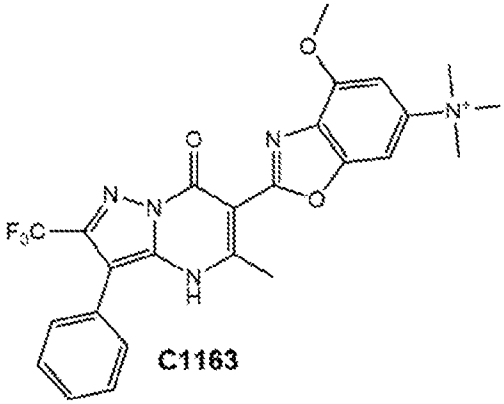
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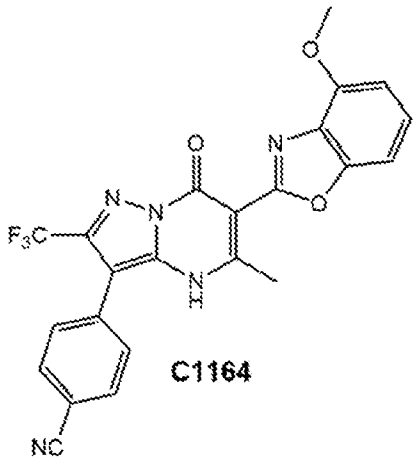
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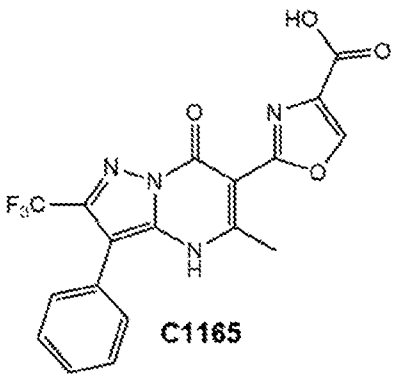
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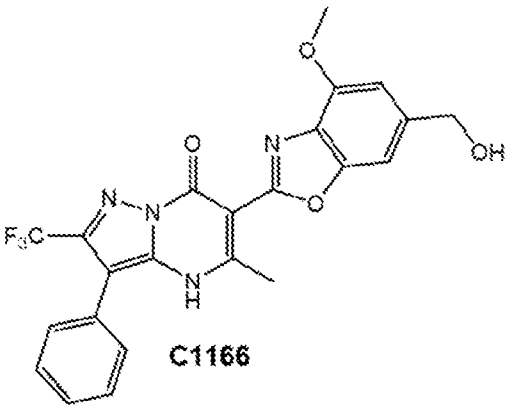
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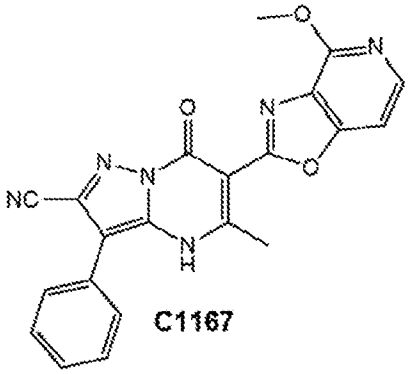
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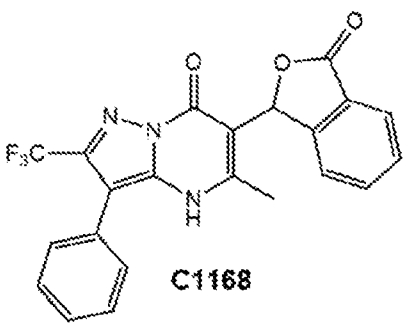
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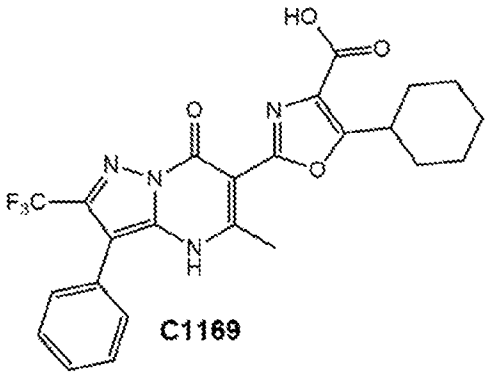
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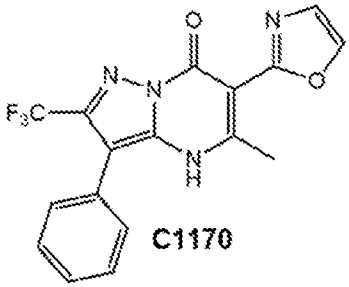


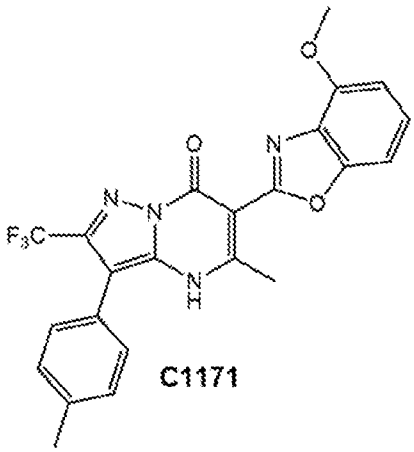
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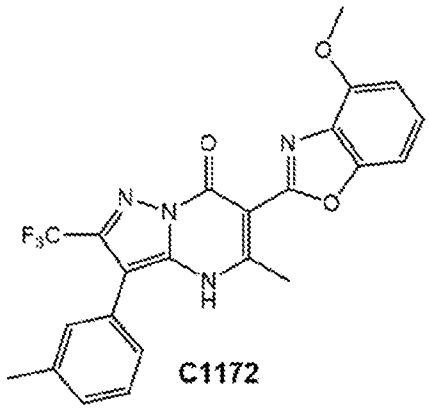


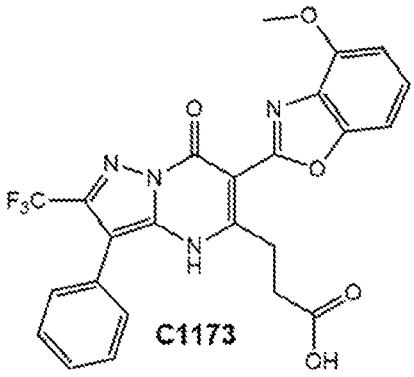
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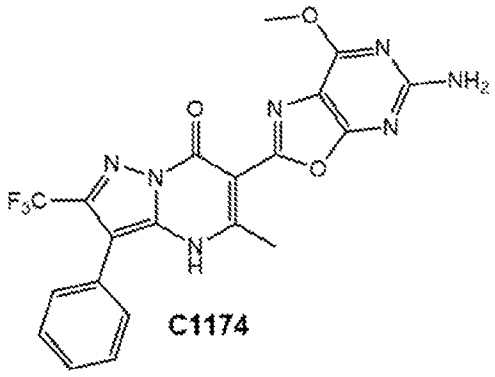

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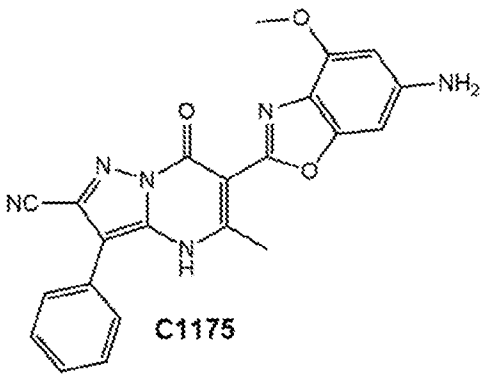

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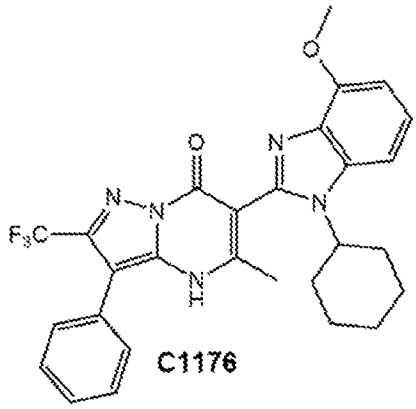

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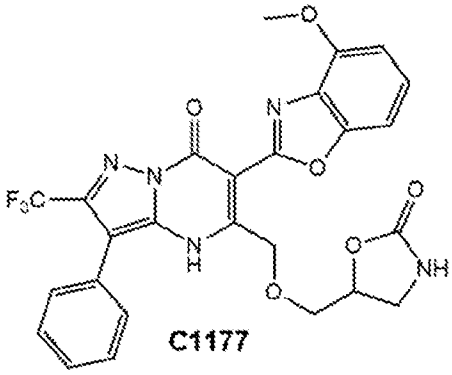

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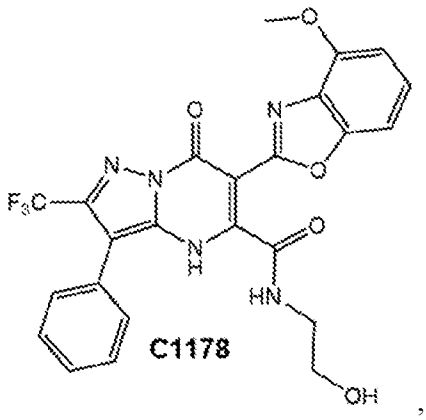

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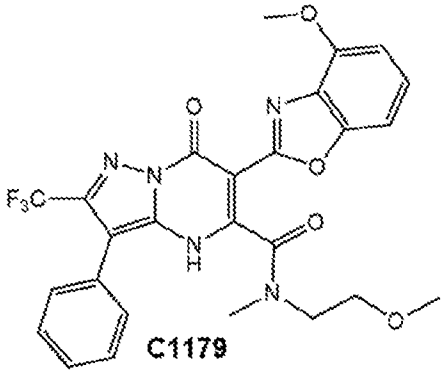

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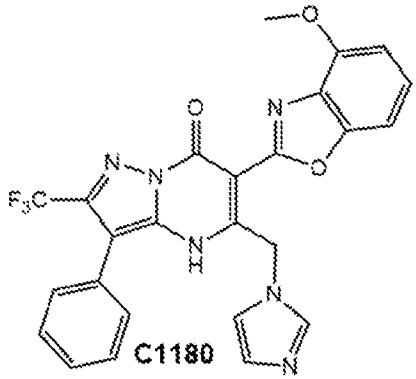

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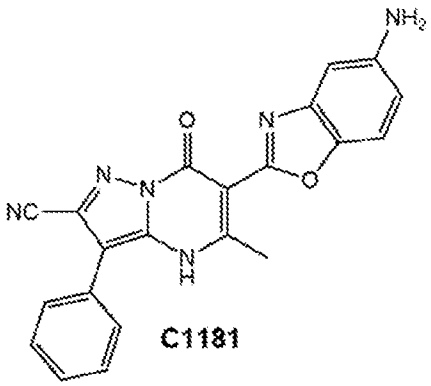

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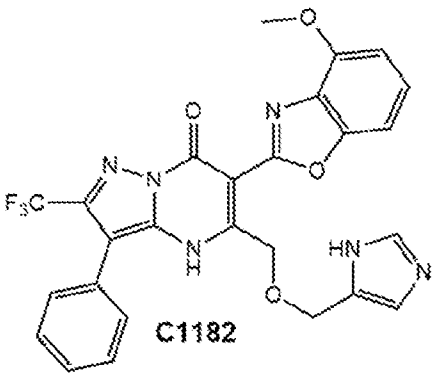

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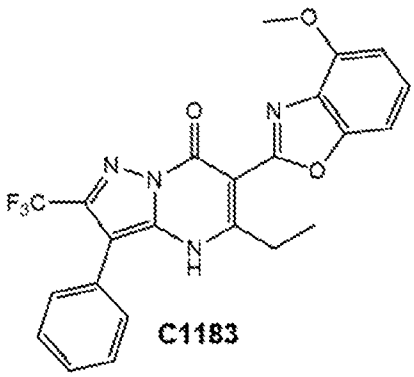

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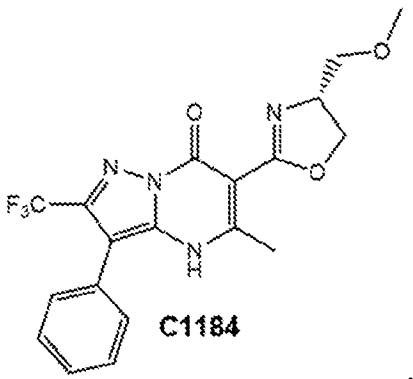

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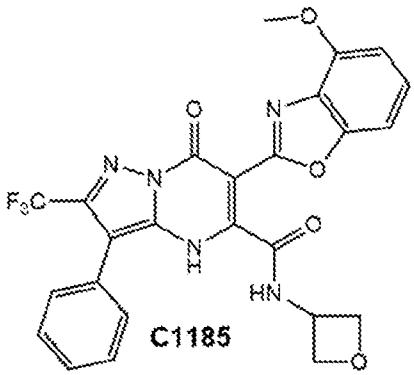

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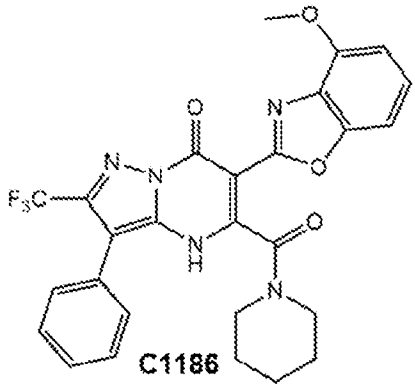

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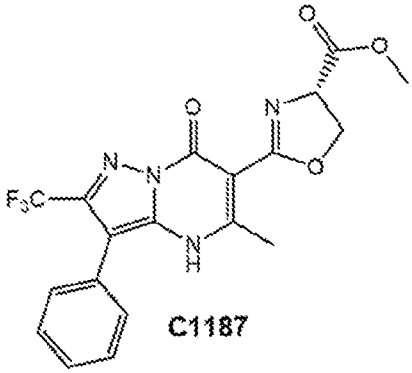

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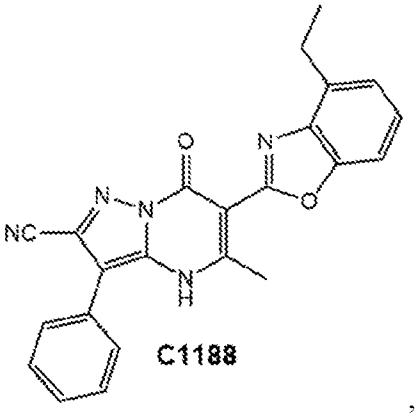

C1183

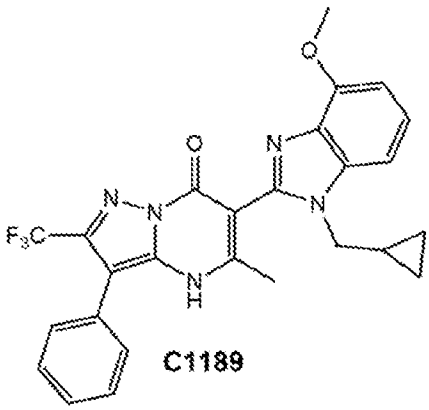

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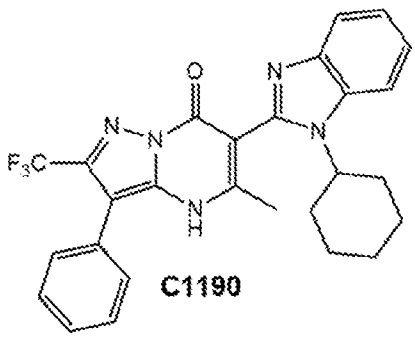

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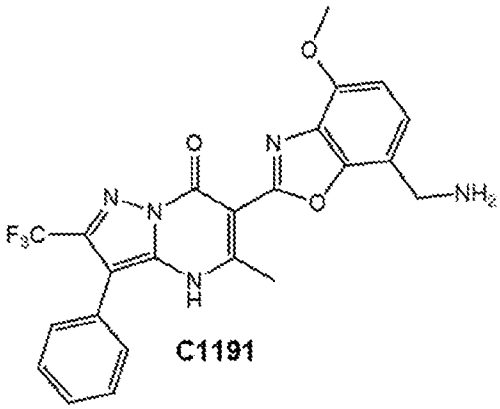

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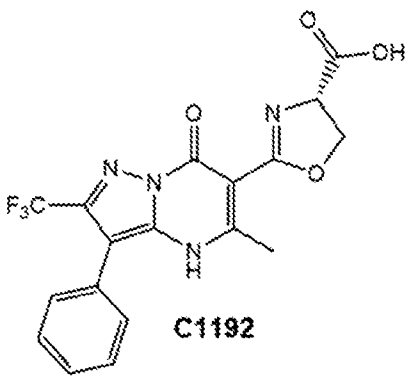

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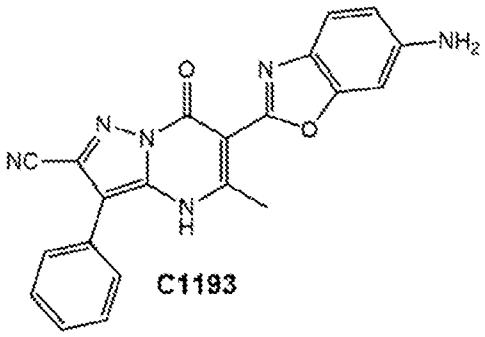

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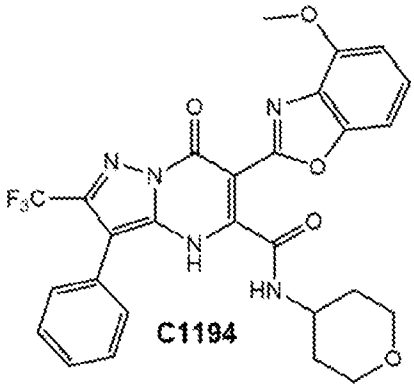

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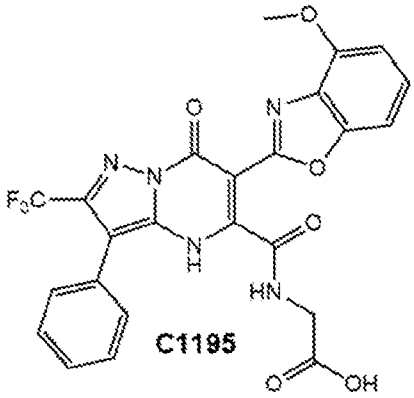

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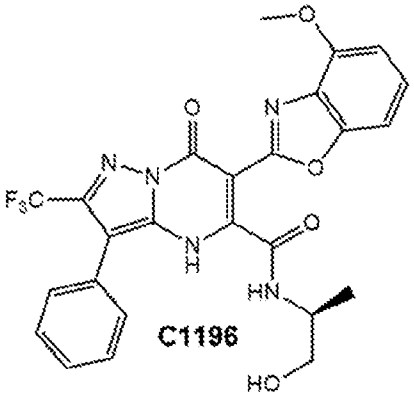

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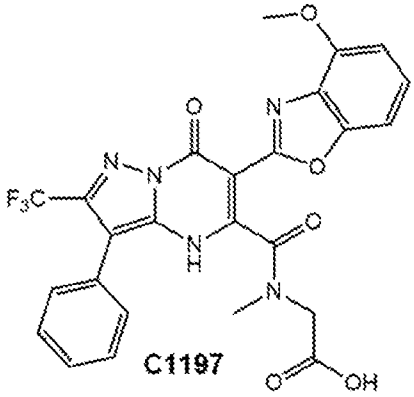

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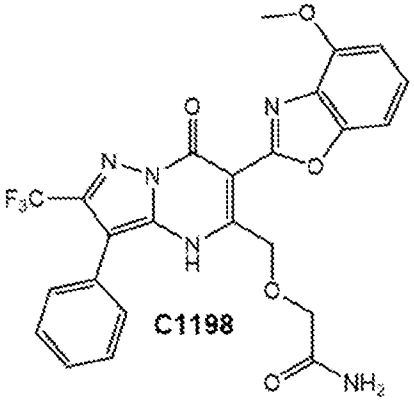

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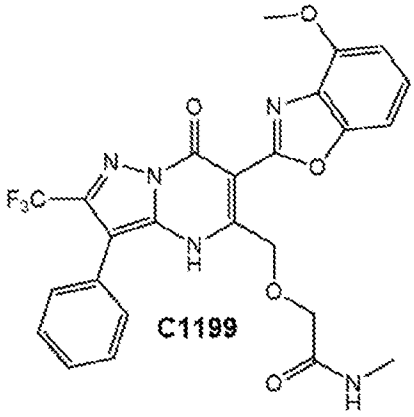

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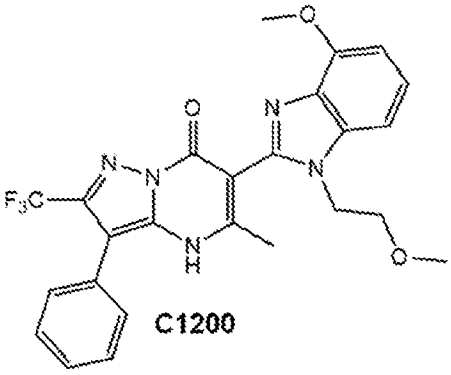

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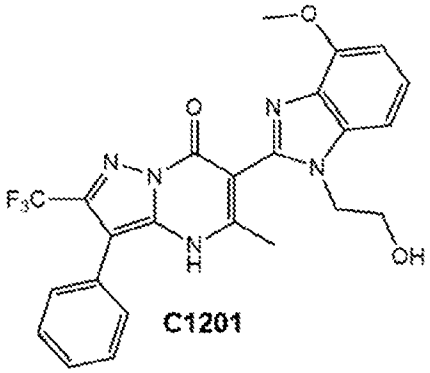

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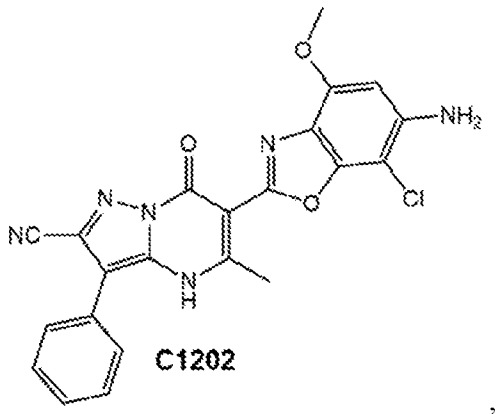

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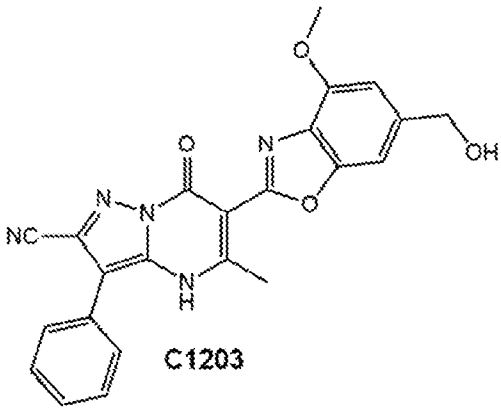

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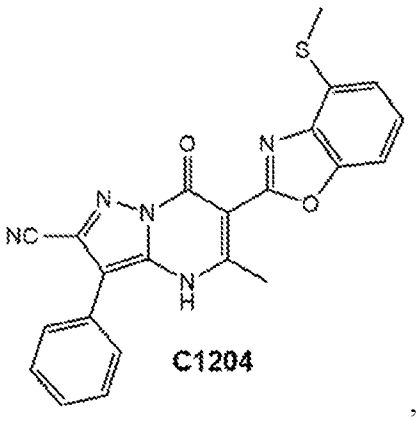
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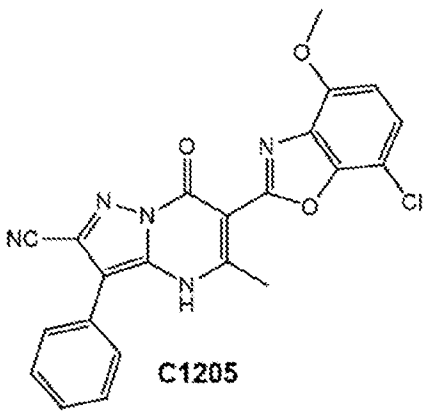
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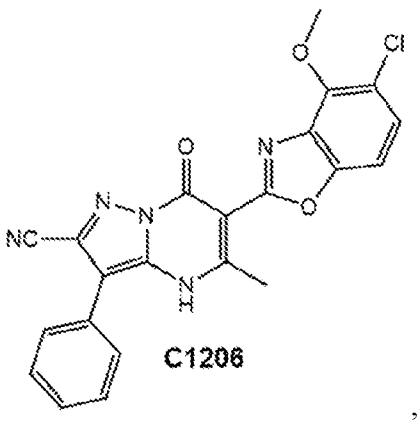
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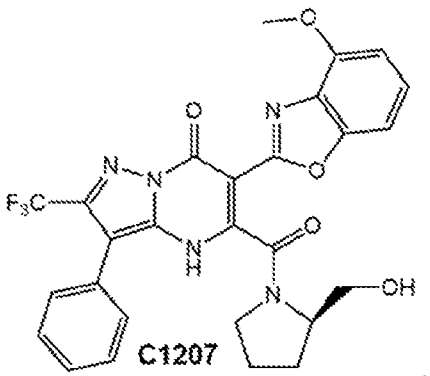
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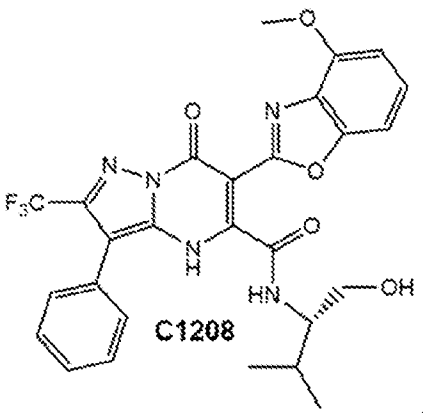
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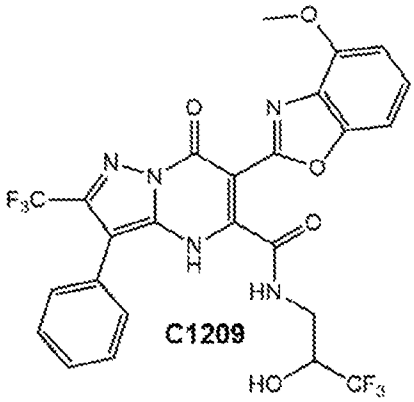
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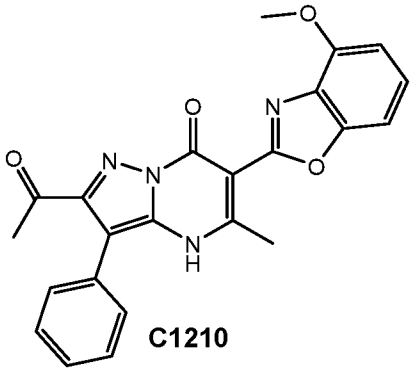


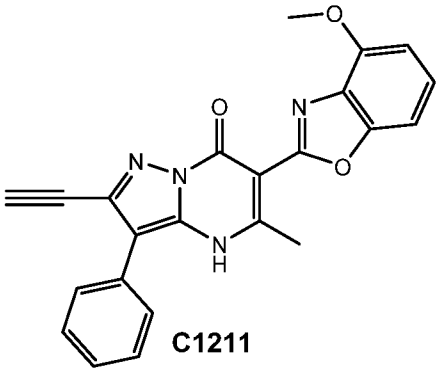
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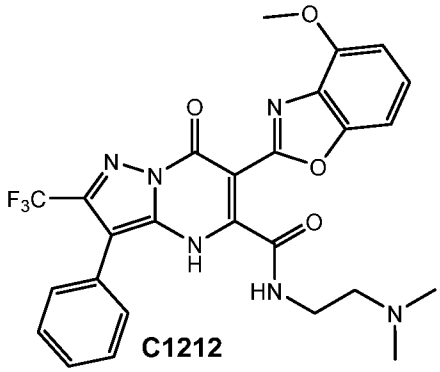


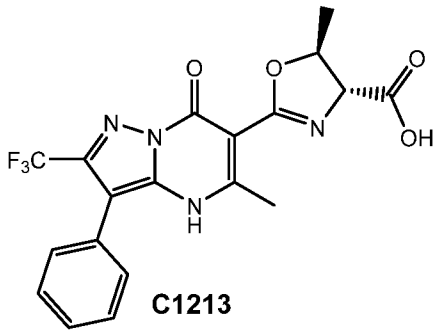
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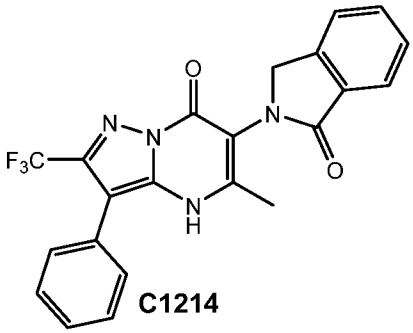

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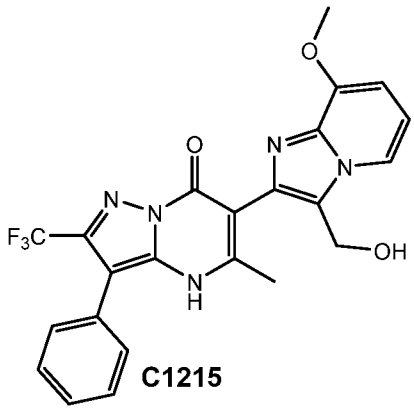

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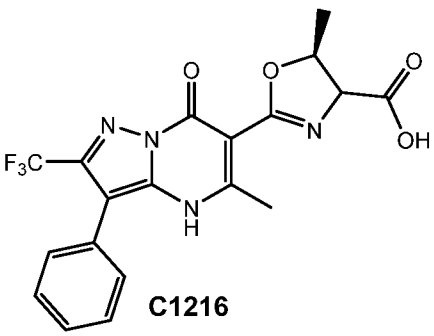

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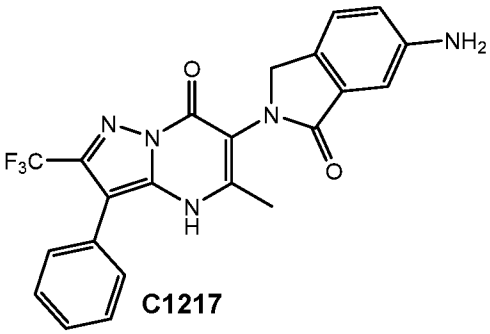

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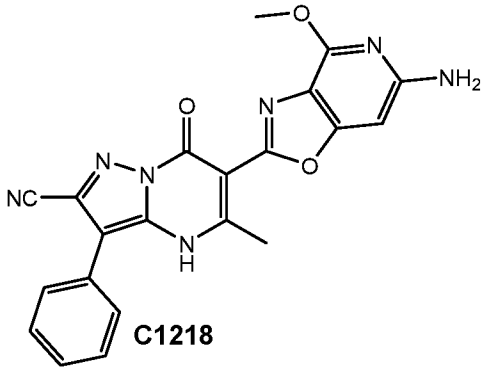

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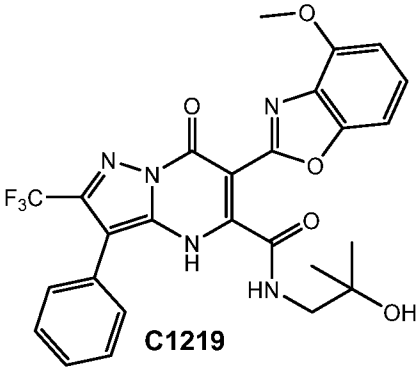

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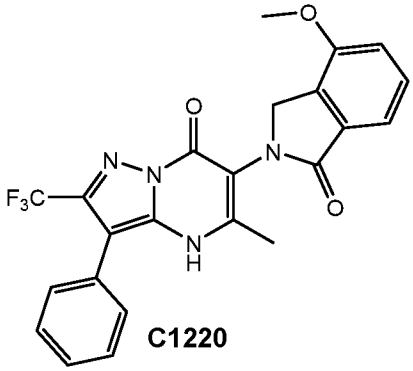

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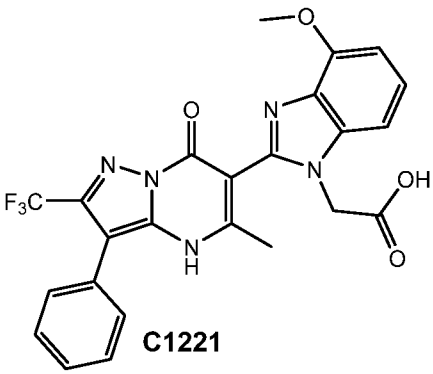

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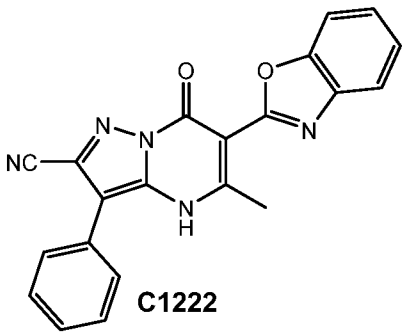

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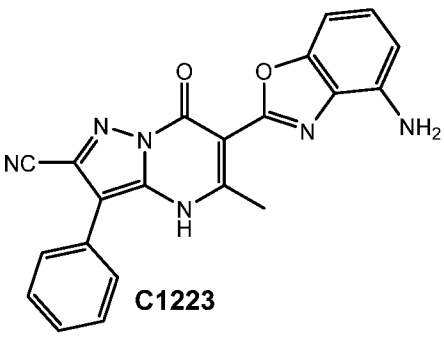

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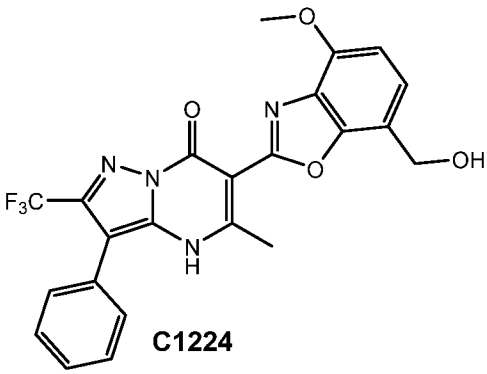

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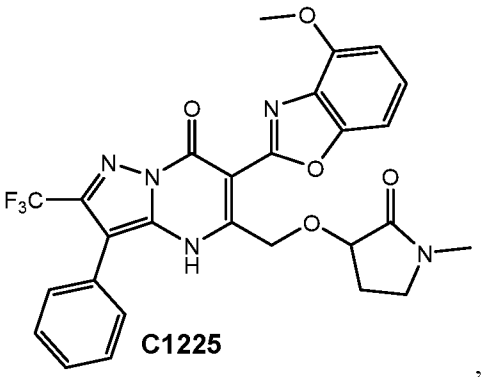

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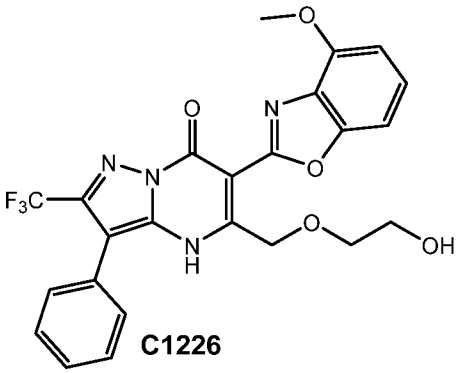

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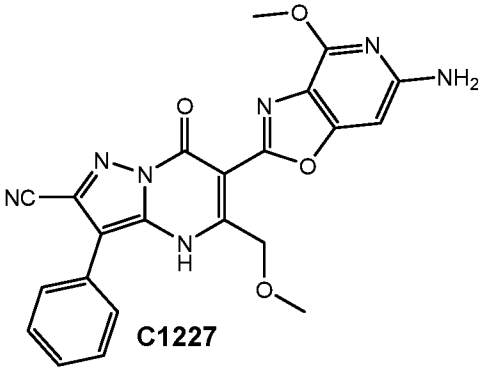

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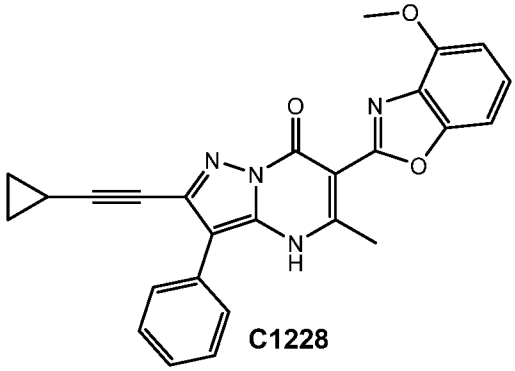

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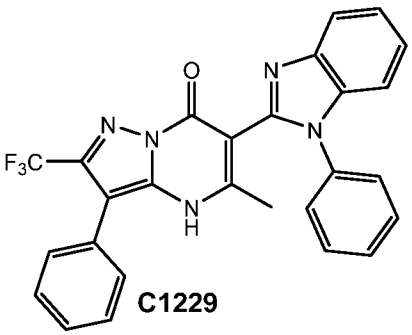

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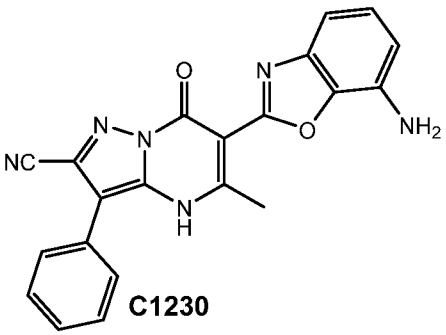

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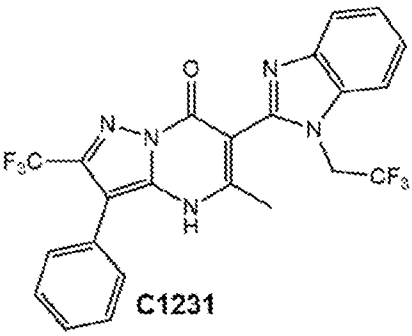

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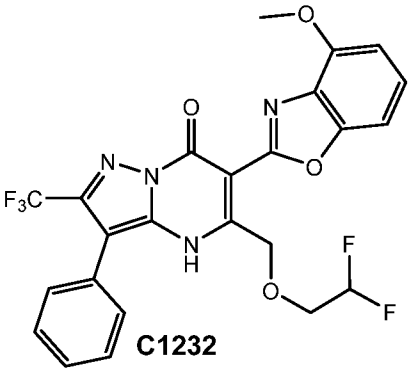

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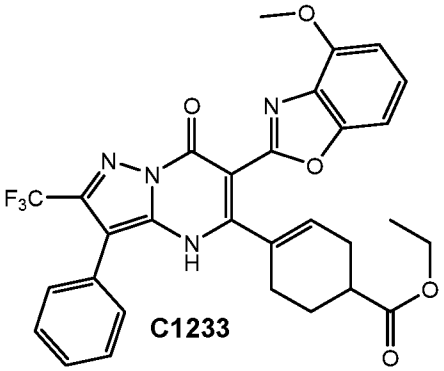

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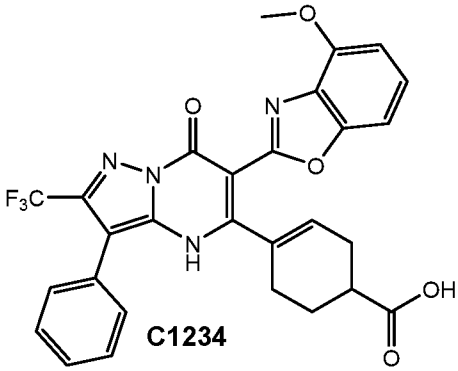

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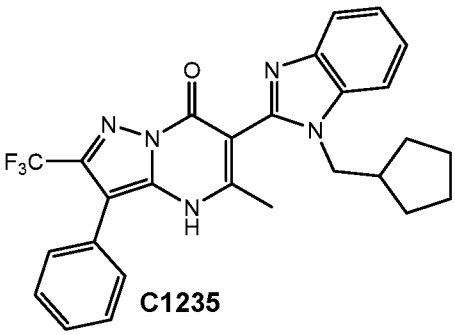

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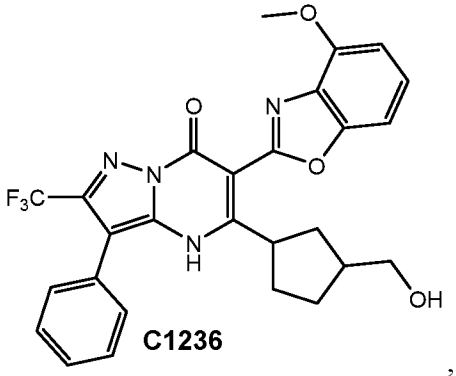

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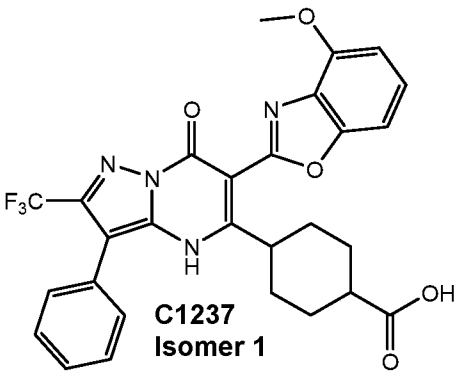

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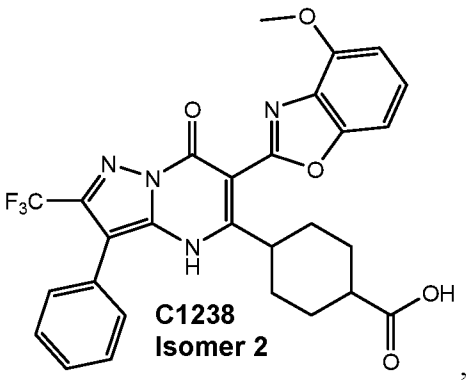

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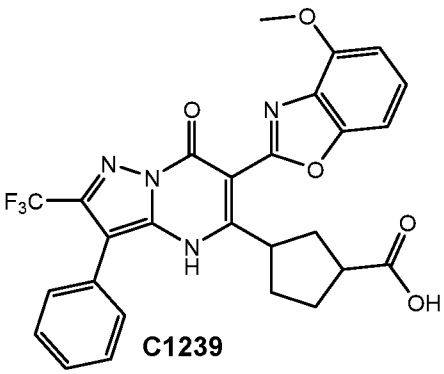

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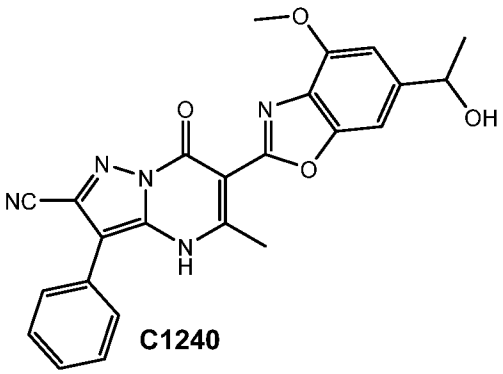

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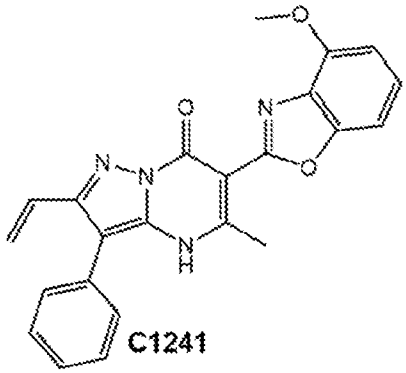

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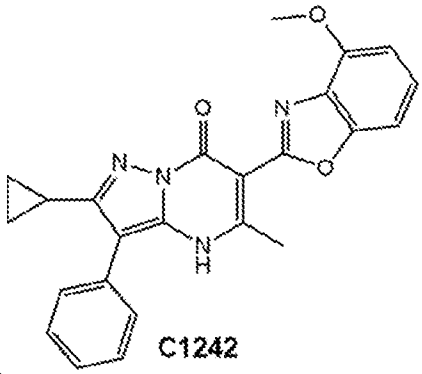

C1237 Isomer 1 ,

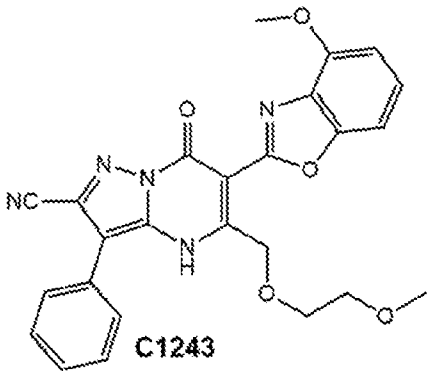

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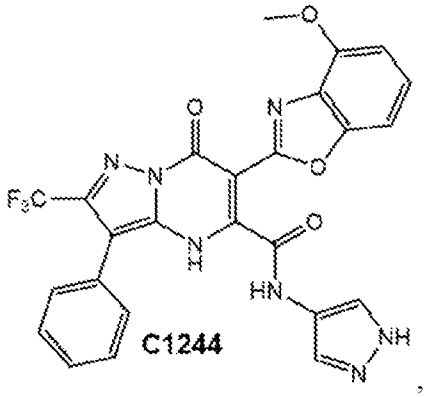

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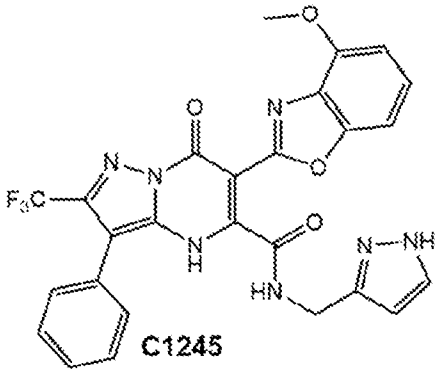

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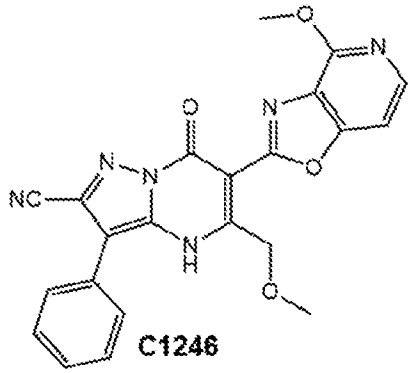

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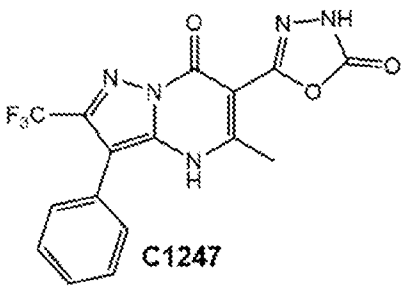

C1242

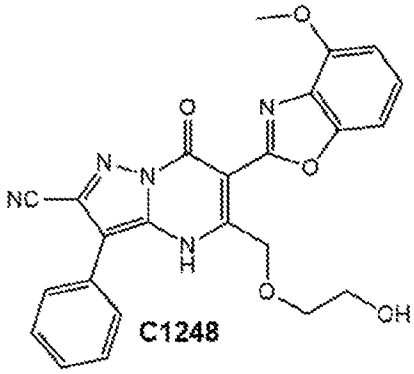

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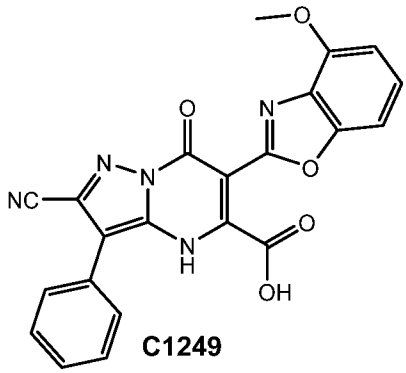

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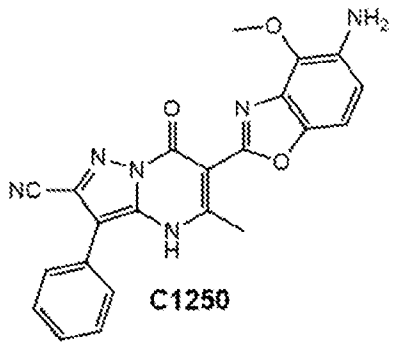

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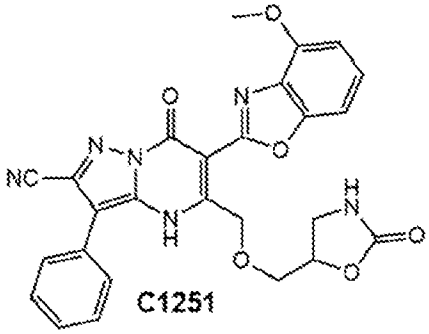

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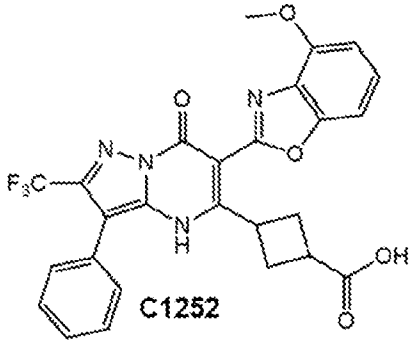

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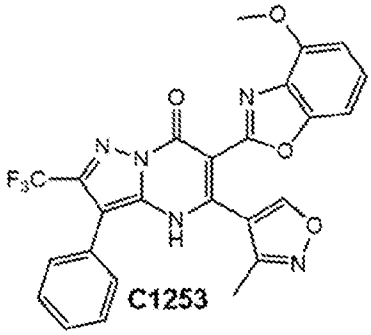

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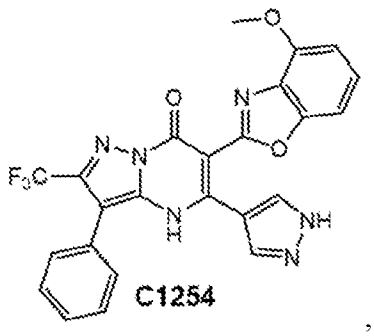

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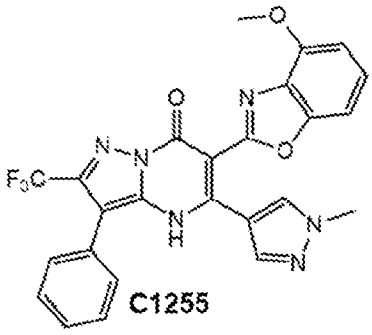

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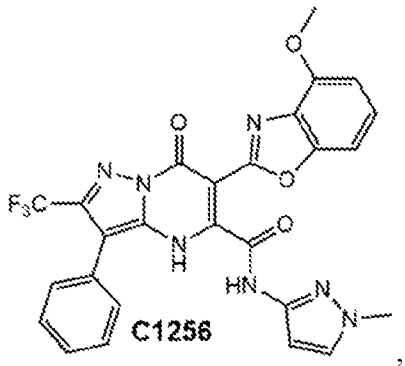

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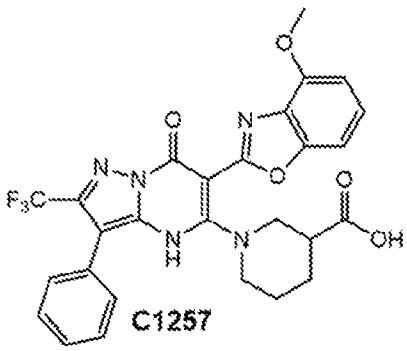

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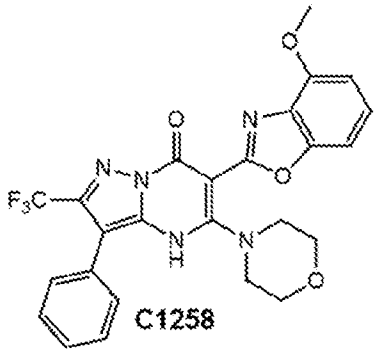

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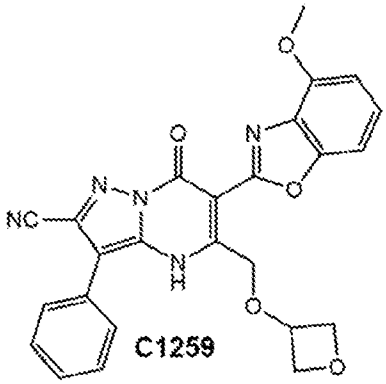

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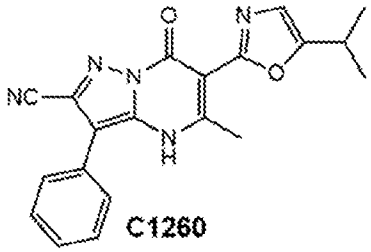

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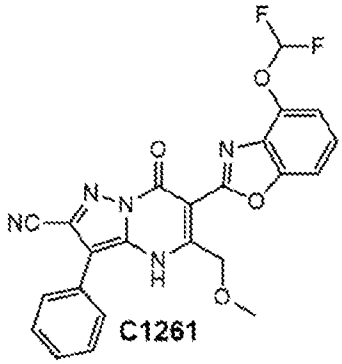

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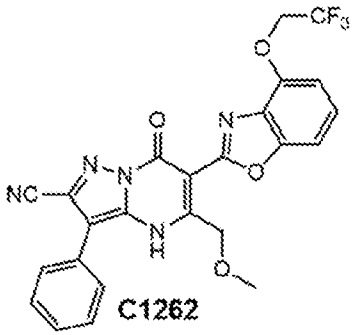

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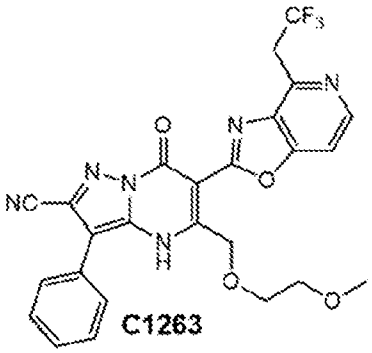

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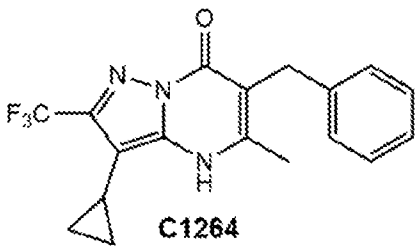

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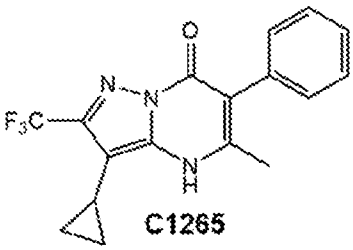

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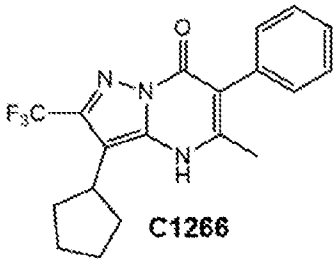

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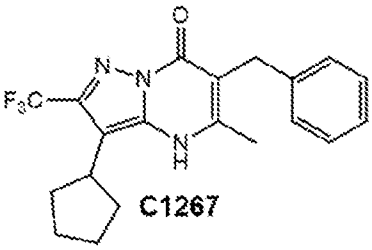

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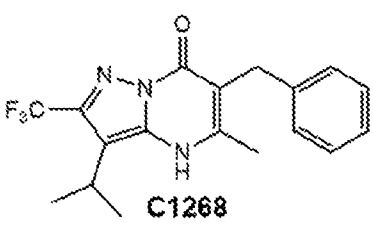

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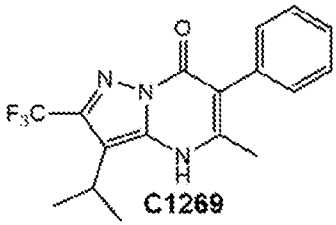

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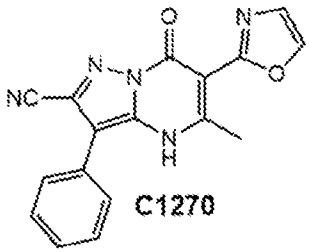

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C1267

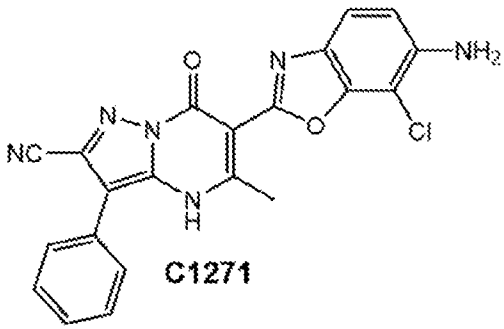

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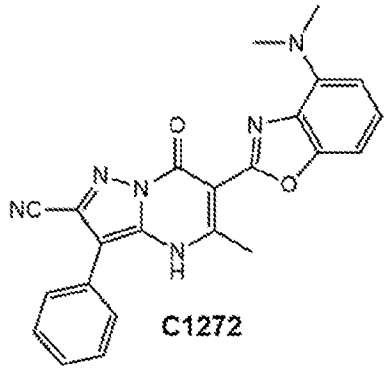
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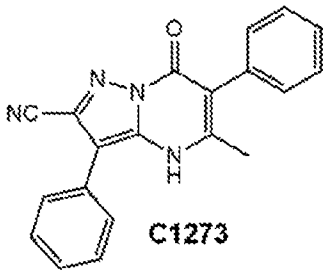
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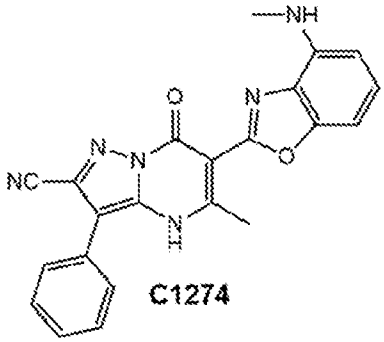
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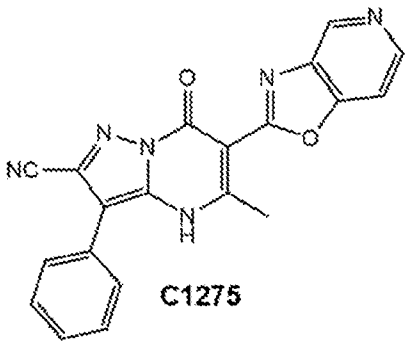
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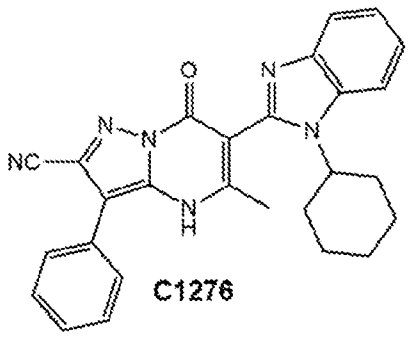
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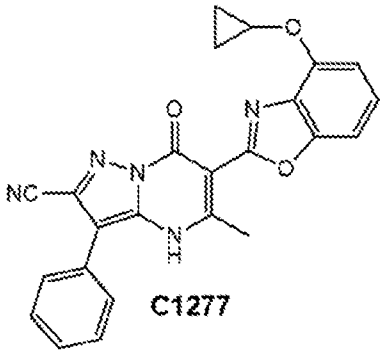
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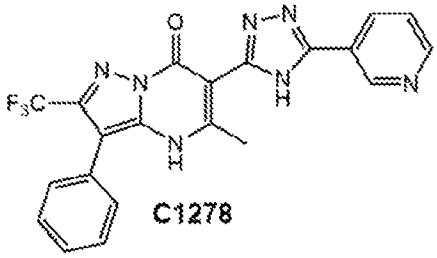
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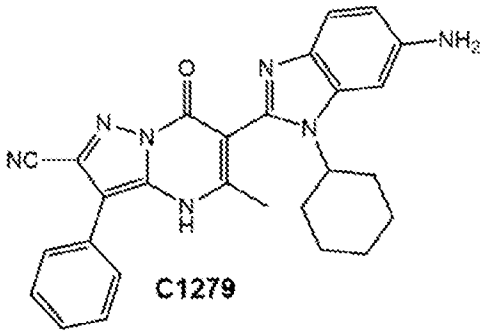
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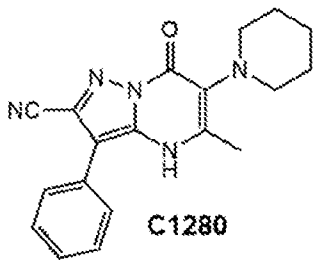
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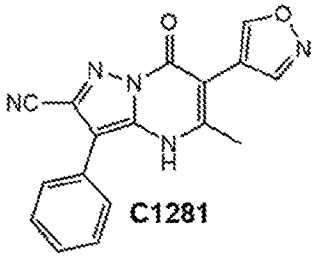
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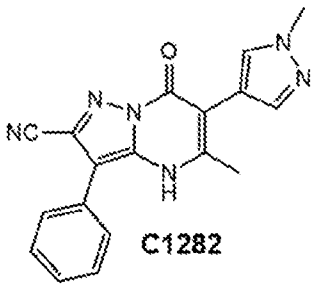
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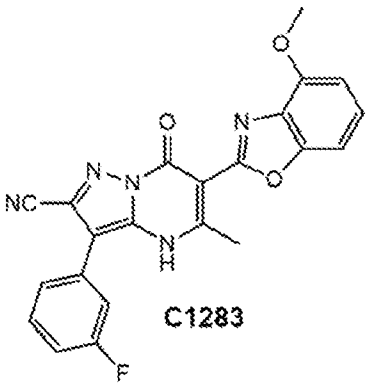
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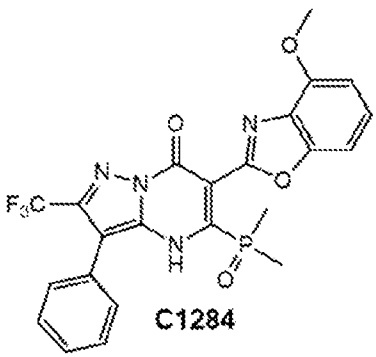
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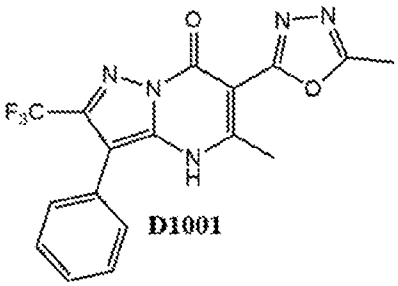
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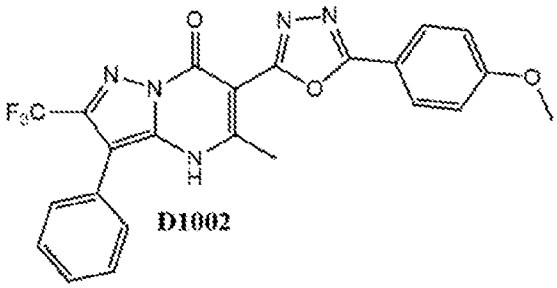
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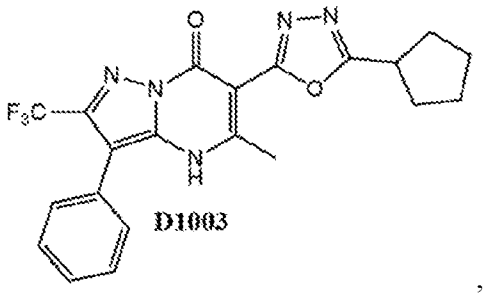
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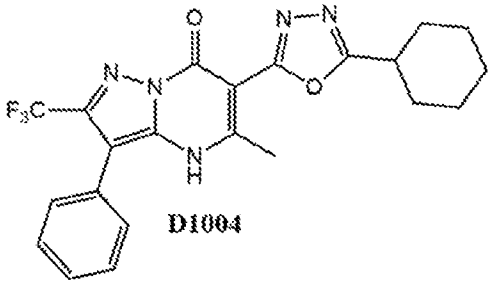
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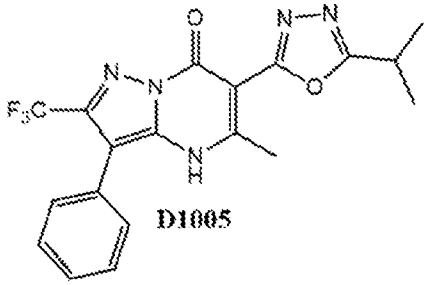
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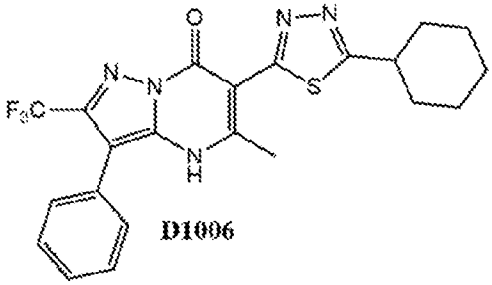
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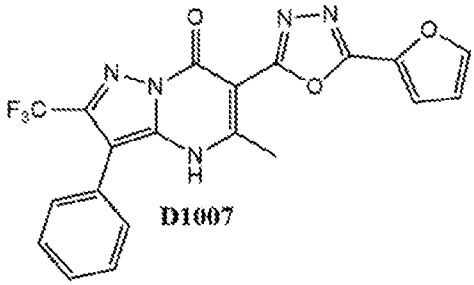
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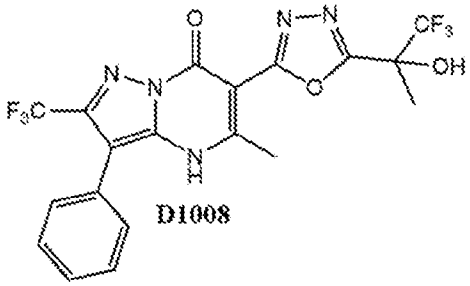
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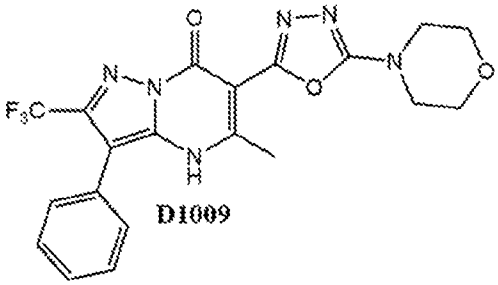
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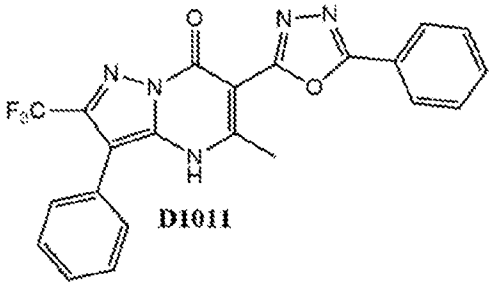
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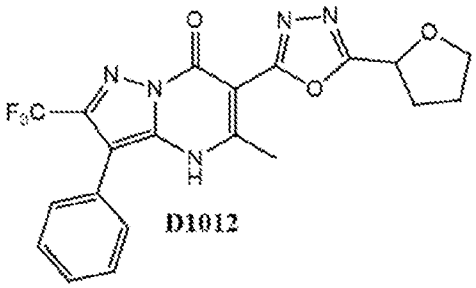
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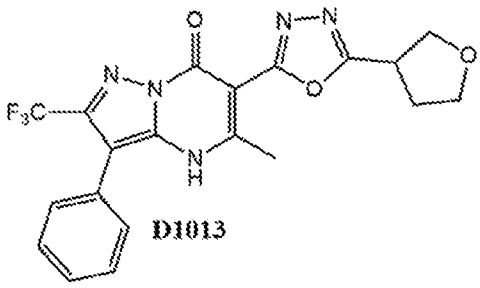


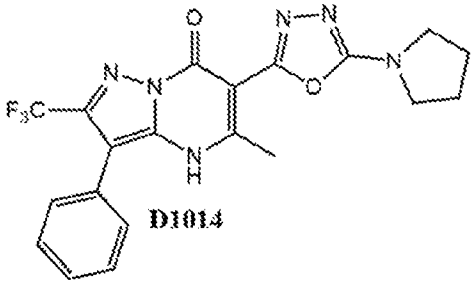
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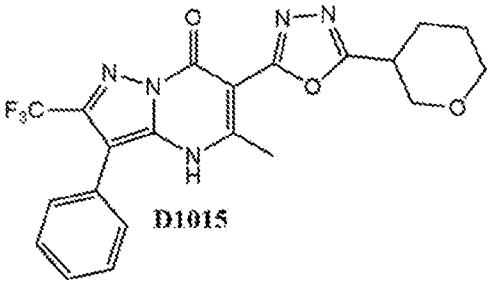


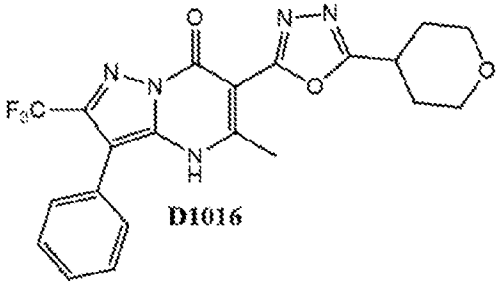
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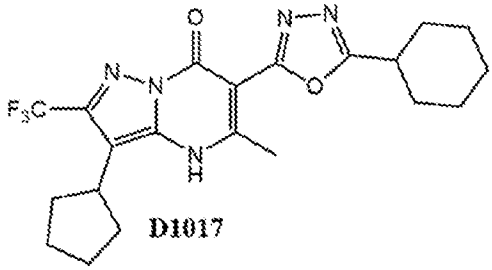

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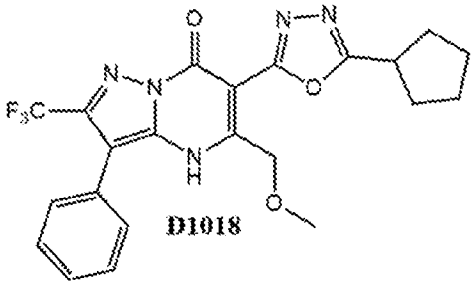

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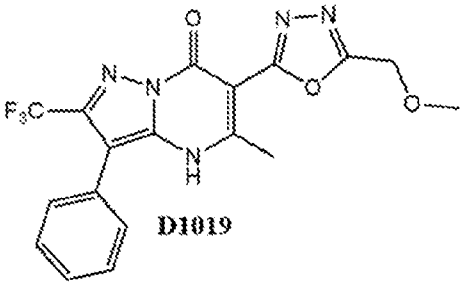

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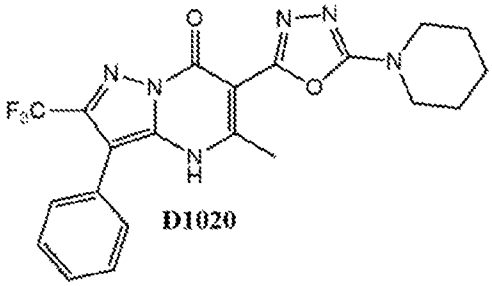

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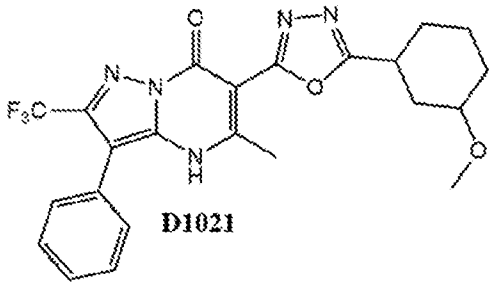

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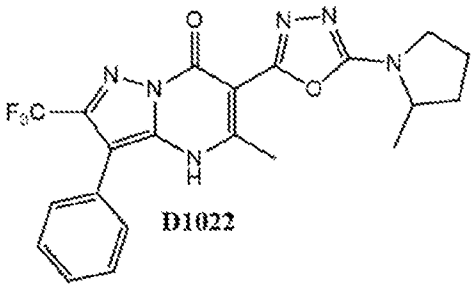

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D1018

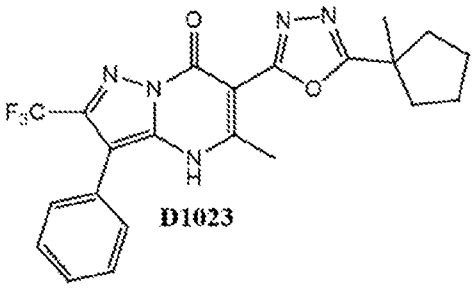

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D1020

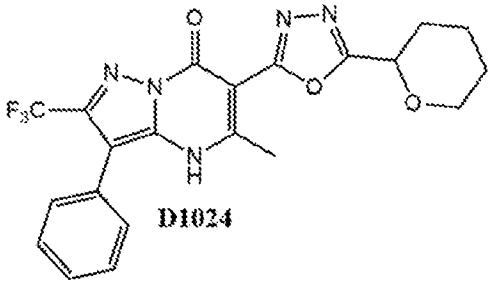

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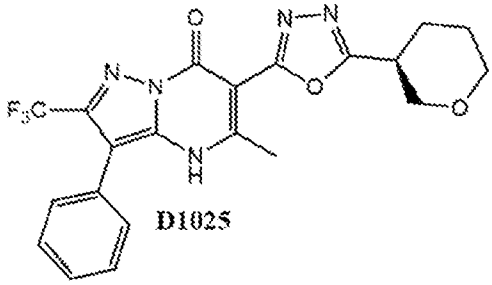
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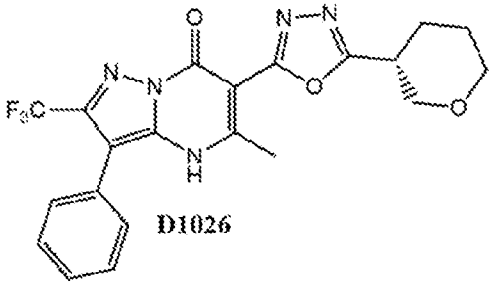
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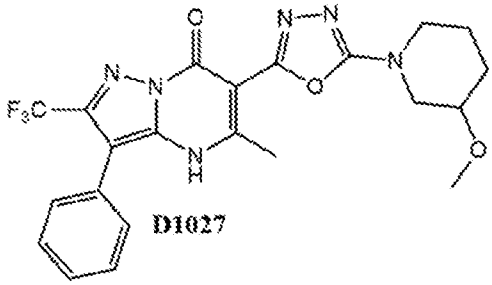
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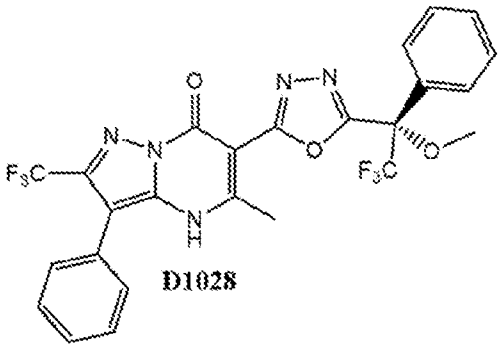
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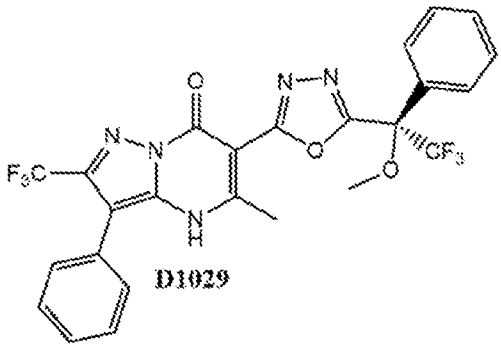
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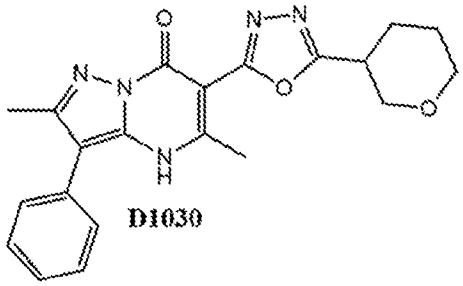
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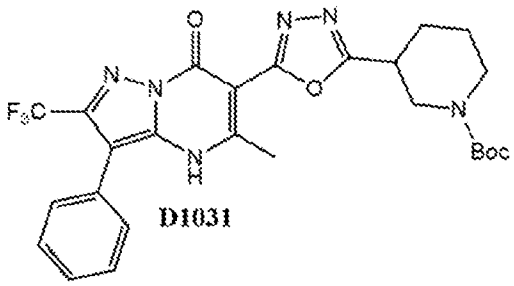
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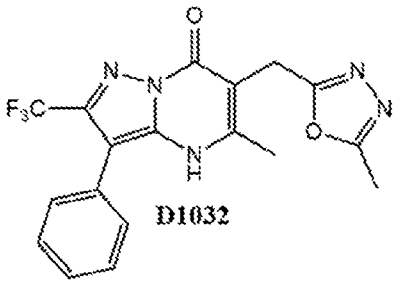
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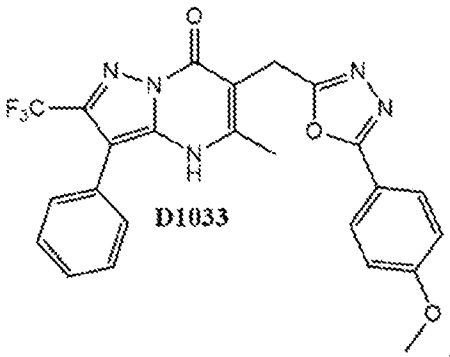
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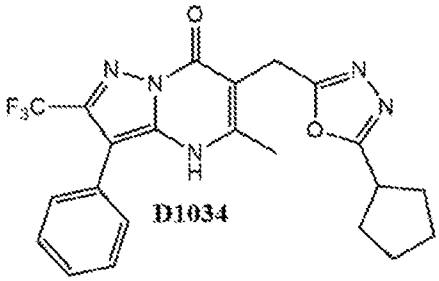
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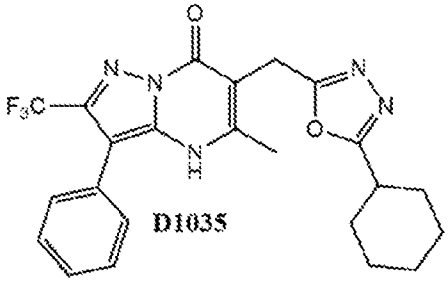
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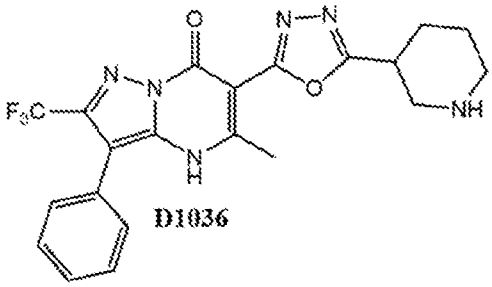
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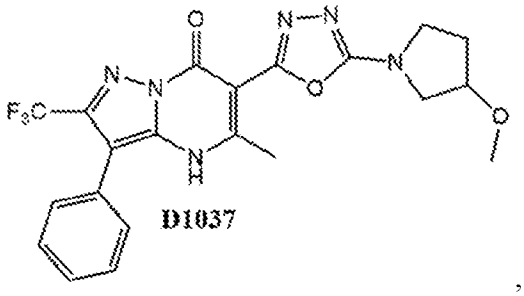
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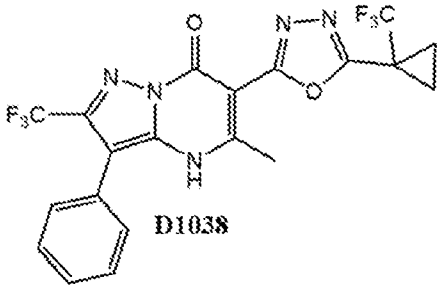
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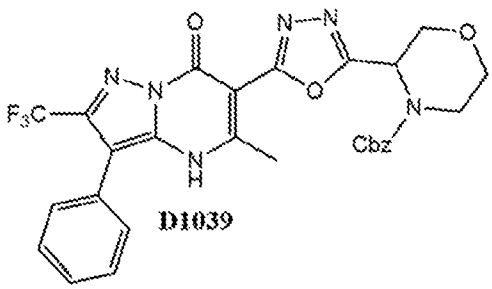
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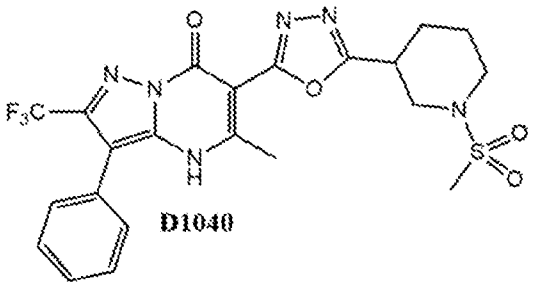
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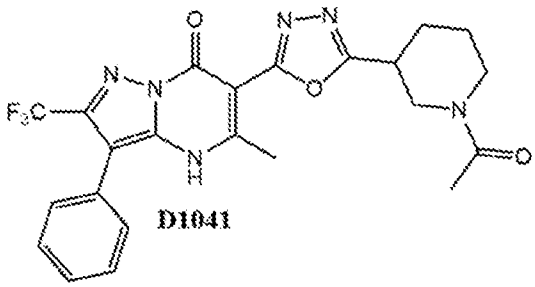
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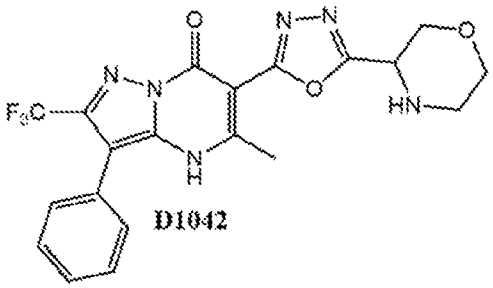
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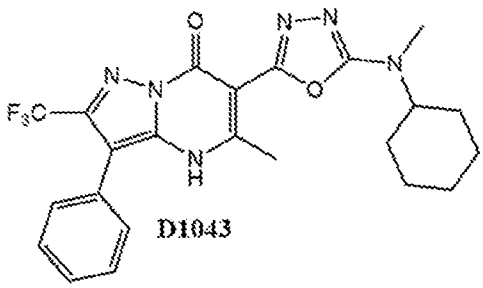


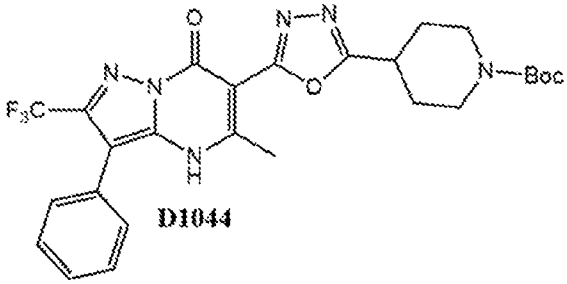
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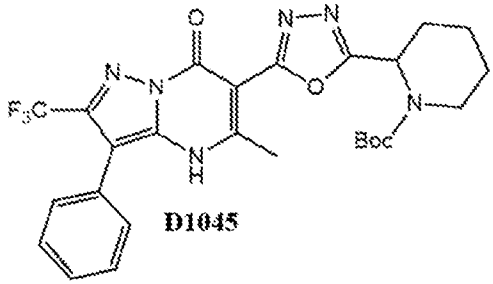


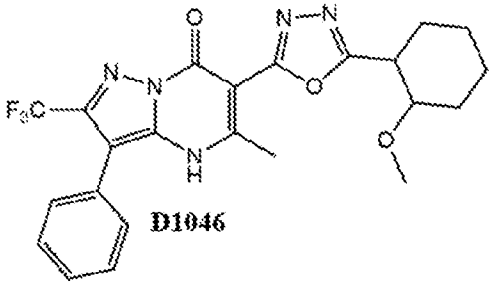
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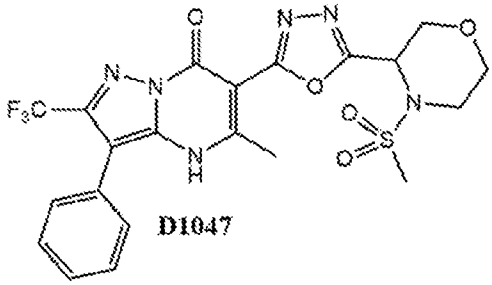

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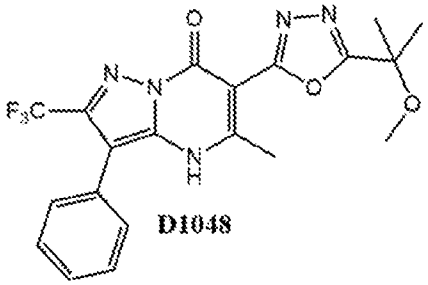

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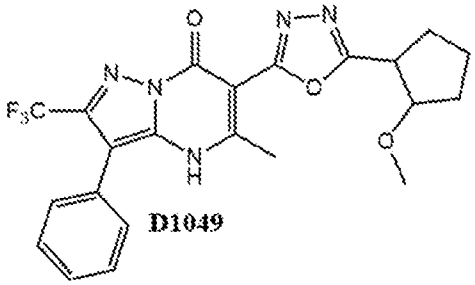

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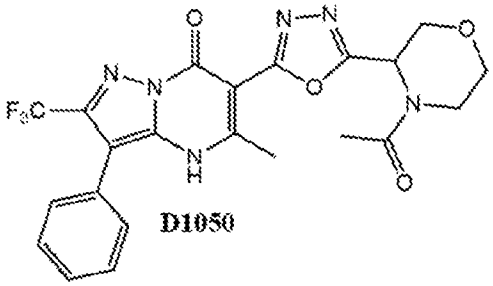

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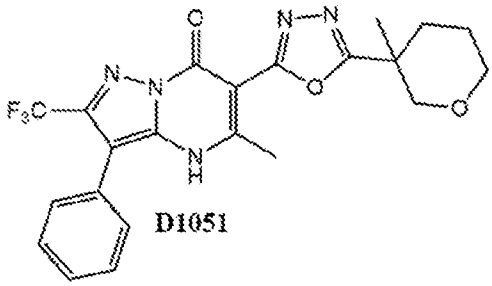

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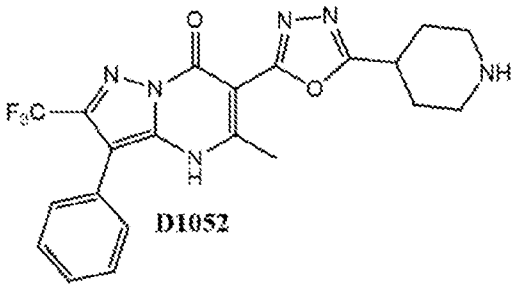

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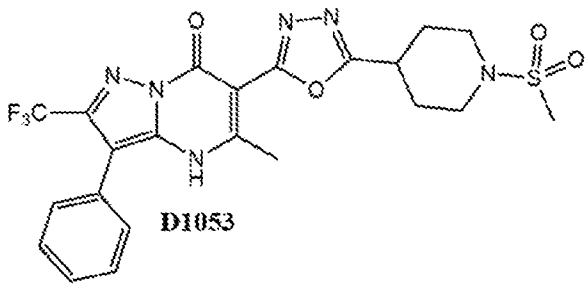

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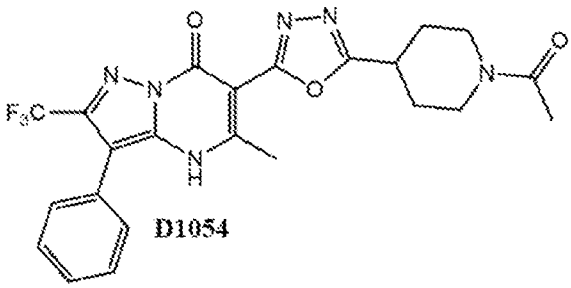

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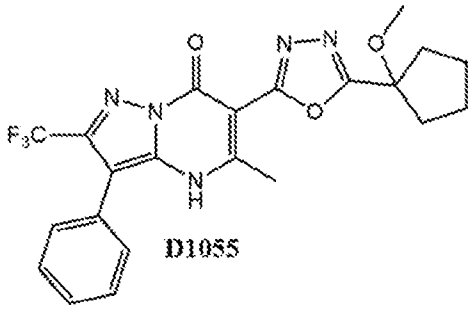
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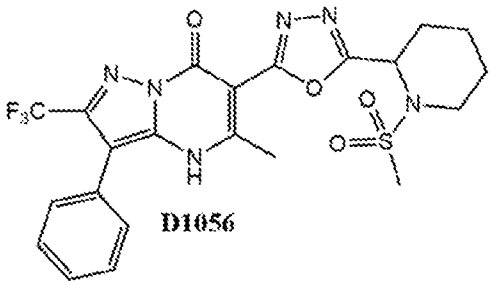
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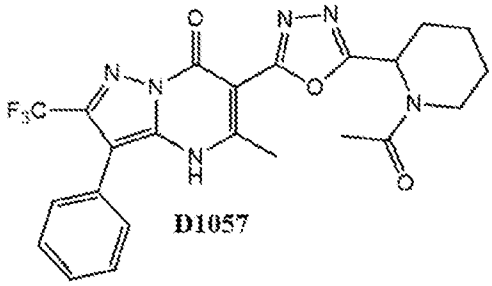
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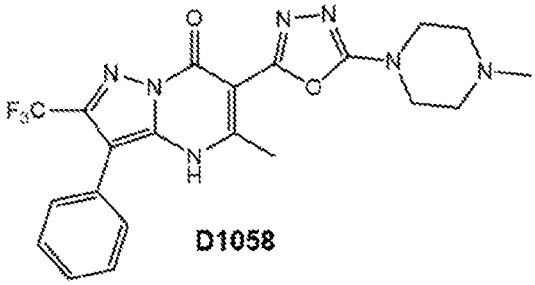
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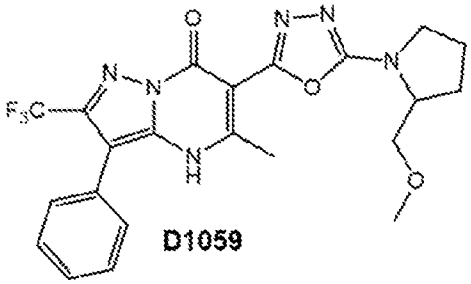
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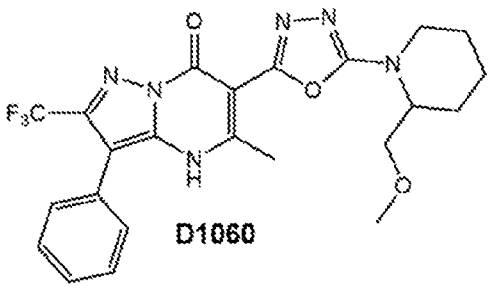
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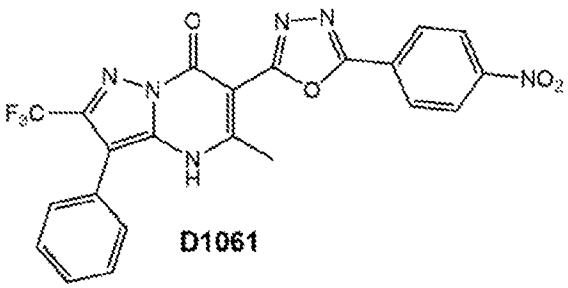
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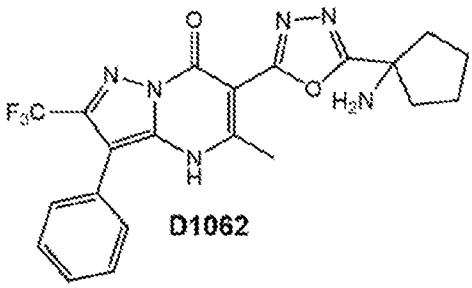
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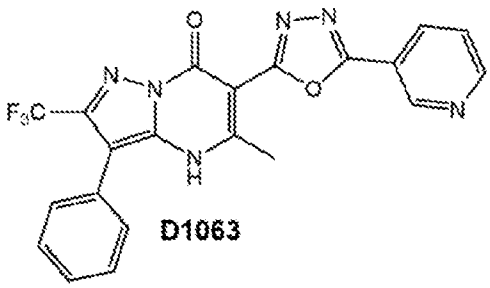


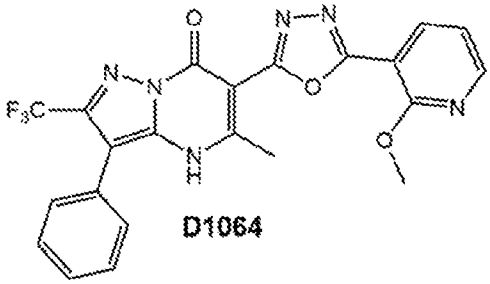
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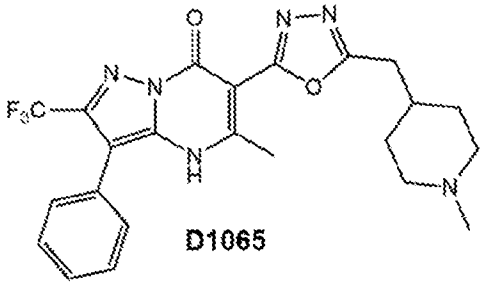


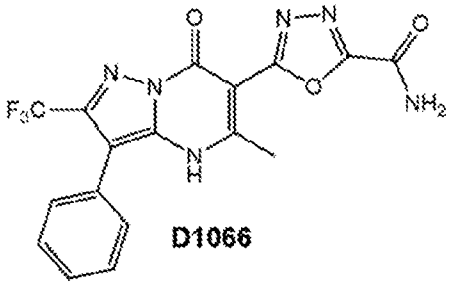
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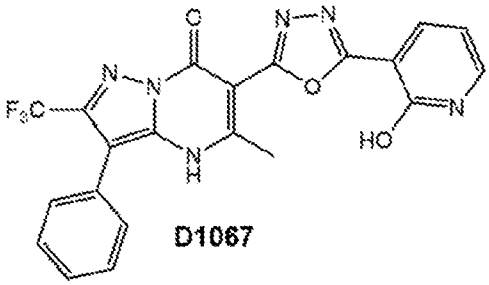

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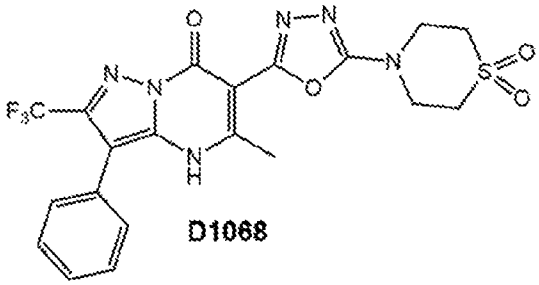

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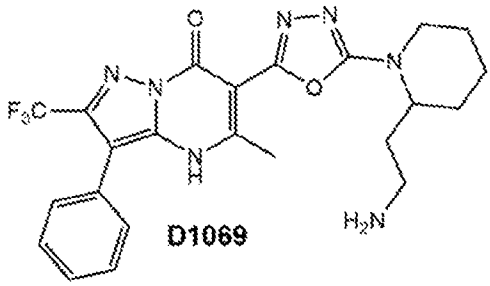

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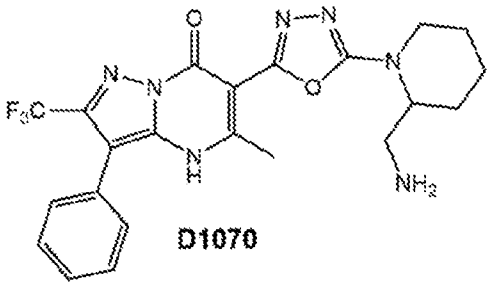

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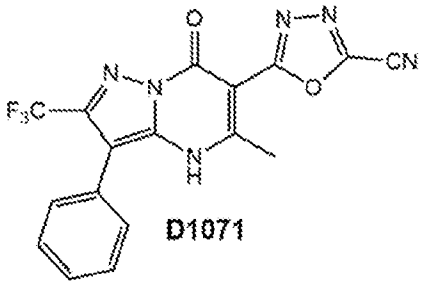

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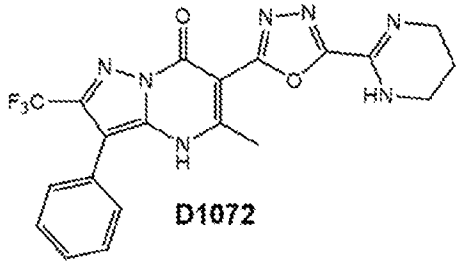

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D1068

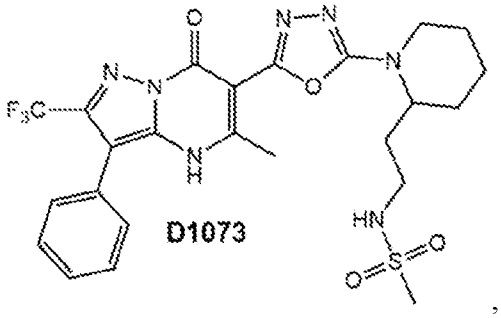

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D1070

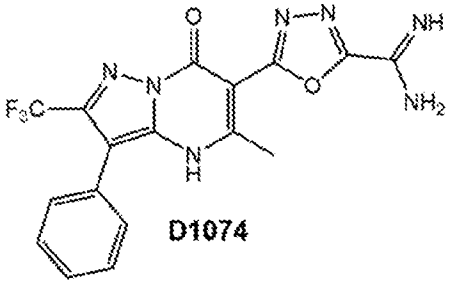

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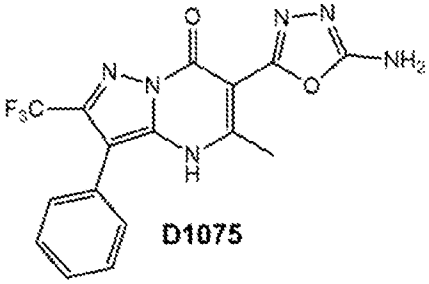
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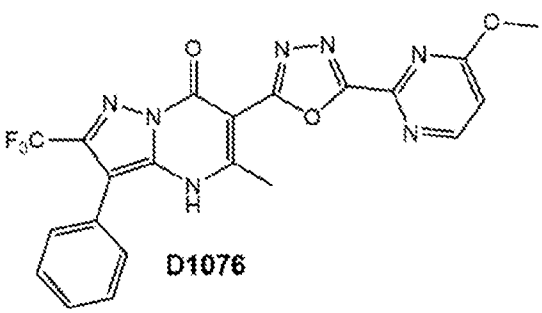
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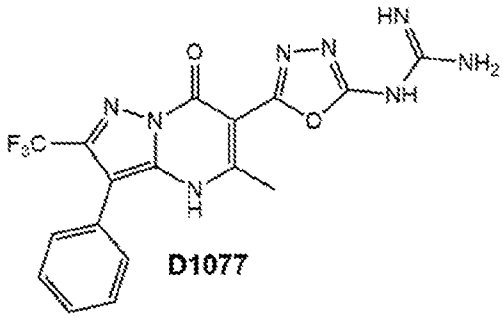
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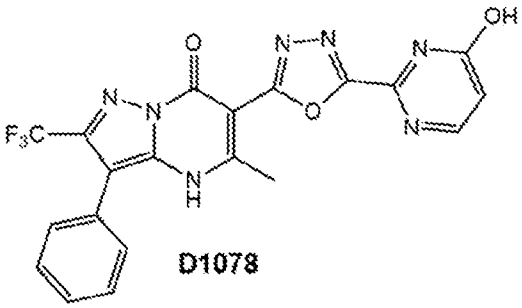
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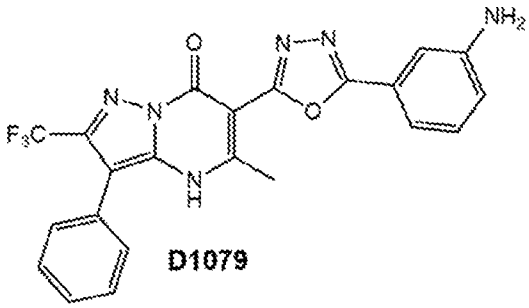
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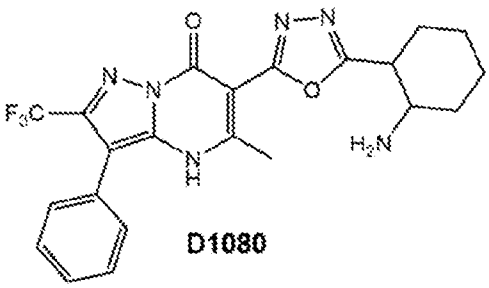
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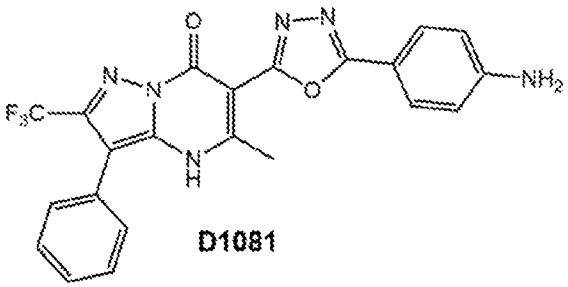
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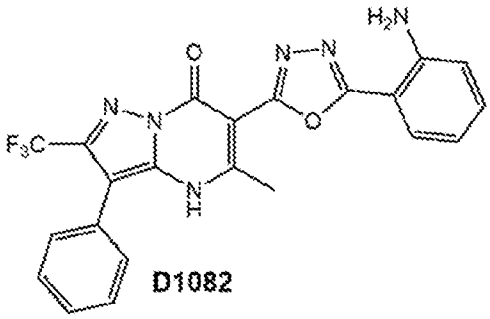
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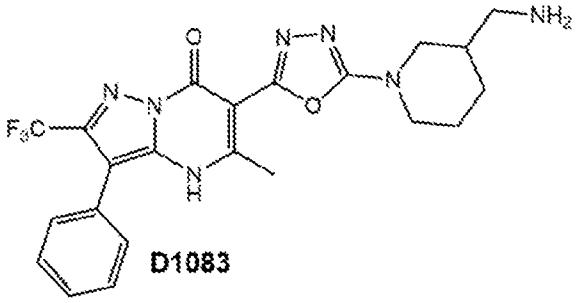


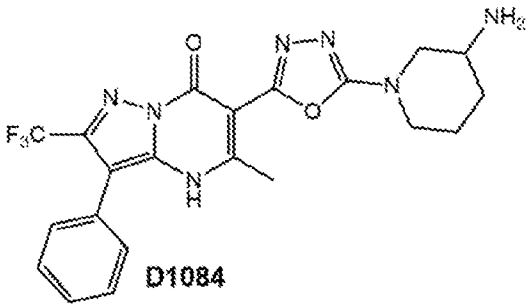
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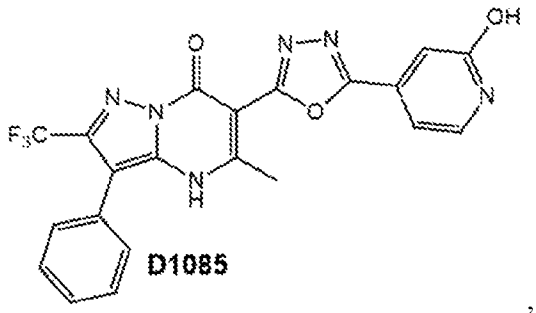


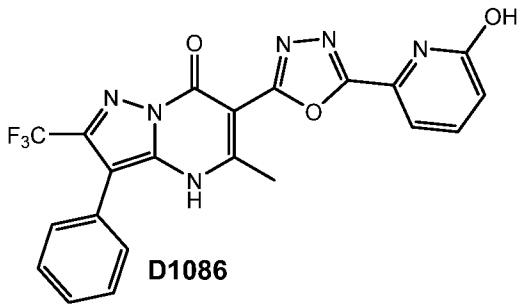
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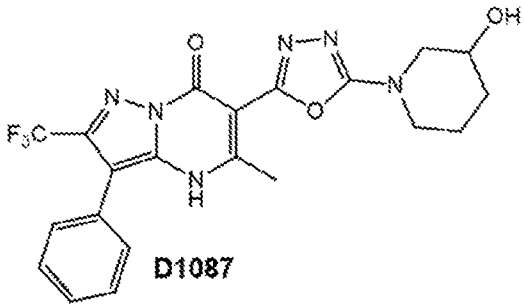

D1082

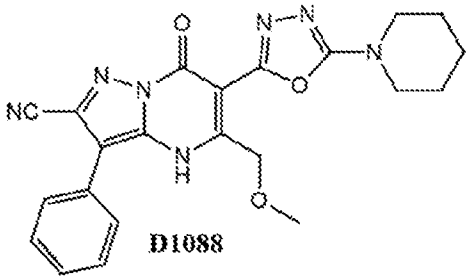

D1083

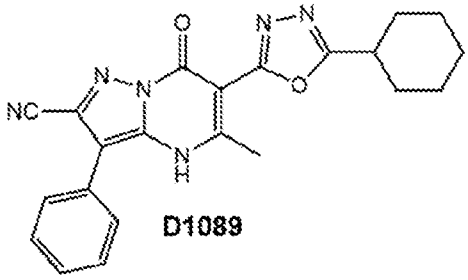

D1084


D1085

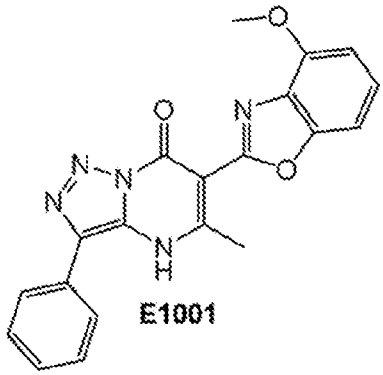

D1086


D1087


D1088


D1089

, and


E1001

,

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

[00261] In one embodiment, the compound is selected from the group consisting of

5-methyl-7-oxo-*N*,3-diphenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1002**);
N-(2-aminophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1006**);
5-methyl-7-oxo-3-phenyl-*N*-(pyridin-2-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1017**);
5-methyl-*N*-(2-(methylsulfonamido)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1022**);
5-methyl-7-oxo-3-phenyl-*N*-(pyrazin-2-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1024**);
5-methyl-7-oxo-3-phenyl-*N*-(thiazol-2-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1028**);
5-methyl-*N*-(1-methyl-1*H*-pyrazol-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1029**);
N-(3-chlorophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1030**);
N-(2-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1031**);
N-(3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1032**);
5-methyl-*N*-(3-(methylsulfonamido)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1045**);
N-(2-(isopropylsulfonyl)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1051**);
N-(4,5-dimethyloxazol-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1056**);
5-methyl-7-oxo-3-phenyl-*N*-(2-(phenylsulfonamido)phenyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1059**);
N-(2,2-difluorobenzo[*d*][1,3]dioxol-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1062**);
N-(6-methoxypyridin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1064**);

N-(1-isopropyl-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1065**);
N-(3-isopropoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1066**);
N-(3,5-dimethoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1067**);
N-(3-aminophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1069**);
N-(3-cyanophenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1070**);
5-methyl-*N*-(oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1074**);
5-methyl-*N*-(5-methyloxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1075**);
5-methyl-7-oxo-3-phenyl-*N*-(1*H*-pyrazol-3-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1076**);
5-methyl-*N*-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1077**);
N-(1,5-dimethyl-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1079**);
5-methyl-*N*-(3-methyl-1*H*-pyrazol-5-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1081**);
N-(3-(cyclopentyloxy)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1082**);
5-methyl-*N*-(2-(methylsulfonyl)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1083**);
5-methyl-*N*-(3-(methylsulfonyl)phenyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1084**);
N-(3-(benzyloxy)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1086**);
N-(2-methoxypyridin-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1087**);

N-(2-methoxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (diastereomer 2) (**A1089**);
N-(4-cyano-1-methyl-1*H*-pyrazol-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1090**);
N-((1*S*,2*S*)-2-hydroxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1091**);
N-(5-methoxypyridin-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1094**);
N-(4-cyclopropylthiazol-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1095**);
5-methyl-*N*-(2-(methylsulfonyl)pyridin-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1096**);
N-(3-methoxypyridin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-6-carboxamide (**A1100**);
N-(2,3-dihydrobenzofuran-7-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1101**);
N-(2,3-dihydrobenzofuran-4-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1102**);
N-(4-methoxypyrimidin-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1104**);
N-(4-methoxypyridin-2-yl)-2,5-dimethyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1105**);
2,5-dimethyl-*N*-(2-(methylsulfonyl)phenyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1106**);
N-(chroman-8-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1107**);
N-(6-methoxypyridazin-3-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1110**);
5-methyl-7-oxo-3-phenyl-*N*-(propylsulfonyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1111**);
N-(benzylsulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1112**);

5-methyl-7-oxo-3-phenyl-*N*-(phenylsulfonyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1116**);
5-methyl-7-oxo-3-phenyl-*N*-(pyridin-2-ylsulfonyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1120**);
N-((2-methoxyphenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1121**);
N-(cyclohexylsulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1124**);
N-((3-methoxyphenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1125**);
N-((2-chlorophenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1127**);
N-((3-cyanophenyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1128**);
N-(3-bromo-5-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1129**);
N-((3-methoxybenzyl)sulfonyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1132**);
N-(3-fluoro-5-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1133**);
N-(3-chloro-5-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1134**);
N-(2-chloro-3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1135**);
N-(2-fluoro-3-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1136**);
N-(3-bromo-5-((dimethylamino)methyl)phenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1139**);
2-cyano-*N*-(6-methoxypyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1144**);
6-(2-((3-methoxyphenyl)amino)ethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1015**);

N-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1*H*-benzo[*d*]imidazol-7-yl)acetamide (**C1009**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1014**);
6-(5-methoxy-1H-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1016**);
5-methyl-3-phenyl-6-(4,5,6,7-tetrahydro-1H-benzo[*d*]imidazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1017**);
6-(4-methoxy-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1018**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1019**);
6-(7-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1022**);
3-isopropyl-5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2(3*H*)-one (**C1023**);
5-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1024**);
8-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1025**);
5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)oxazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1027**);
5-methyl-6-(oxazolo[4,5-b]pyridin-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1030**);
2,5-dimethyl-3-phenyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1032**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-6,7-dihydrobenzo[d]oxazol-4(5*H*)-one (**C1033**);
6-(4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1037**);
6-(4-ethoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1038**);

6-(4-isopropoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1039**);
6-(4-bromobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1040**);
6-(4-(2-methoxyethoxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1041**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-2,5-dimethyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1042**);
6-(8-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1044**);
6-(4-(cyclopropylmethoxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1045**);
6-(4-ethylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1046**);
5-methyl-6-(4-(methylthio)benzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1047**);
6-(4-methoxy-4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1048**);
2-(difluoromethyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1050**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1051**);
6-(4-hydroxy-4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1052**);
6-(4-hydroxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1053**);
6-(4-chlorobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1055**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(methoxymethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1056**);
6-(5-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1057**);

6-(7-methoxyoxazolo[5,4-*b*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1058**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-5,6,7,8-tetrahydro-4*H*-oxazolo[4,5-*c*]azepin-4-one (**C1059**);
5-methyl-6-(4-methylbenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1060**);
N-(2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl)oxy)ethyl)acetamide (**C1062**);
N-(2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl)oxy)ethyl)methanesulfonamide (**C1066**);
6-(4-methoxybenzo[*d*]thiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1070**);
5-chloro-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1071**);
6-(4-(benzyloxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1073**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazole-4-carbonitrile (**C1075**);
6-(4-fluorobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1076**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2,5-bis(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1077**);
6-(4-(dimethylamino)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1078**);
6-(7-bromo-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1081**);
6-(5-bromo-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1082**);
5-methoxy-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1084**);
5-amino-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1085**);

2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl dimethylcarbamate (**C1088**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carbonitrile (**C1089**);
3-(2-fluorophenyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1091**);
6-(4-methoxy-7-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1092**);
6-(4-methoxy-5-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1093**);
6-(7-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1094**);
6-(5-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1095**);
6-(7-methoxyoxazolo[5,4-*c*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1096**);
5-methyl-6-(4-(methylsulfinyl)benzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1097**);
6-(4-methoxy-6-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1098**);
5-((benzyloxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1099**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazole-7-carbonitrile (**C1100**);
ethyl 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazole-4-carboxylate (**C1101**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazole-4-carboxamide (**C1102**);
5-(hydroxymethyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1103**);
6-(4-(hydroxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1104**);

6-(6-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1105**);
5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazolo[4,5-*c*]pyridin-4(5*H*)-one (**C1106**);
6-(4-(methoxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1108**);
5-((dimethylamino)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1109**);
6-(7-acetyl-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1111**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-7-carboxamide (**C1113**);
3-(3-fluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1114**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazolo[4,5-c]pyridin-4(5H)-one (**C1116**);
2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-4-yl)oxy)acetic acid (**C1117**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-5-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1118**);
3-(3,5-difluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1119**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(methylthio)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1121**);
2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-4-yl)oxy)acetamide (**C1122**);
6-(6-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1123**);
6-(4-methoxy-7-(methylsulfonyl)benzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1125**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-5-carbonitrile (**C1126**);

6-(6-(aminomethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1128**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid (**C1130**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid (**C1131**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1132**);
6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1134**);
6-(6-(aminomethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (HCl salt) (**C1135**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylthio)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1136**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylsulfinyl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1137**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylsulfonyl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1138**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1139**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboximidamide (**C1141**);
6-(4-methoxybenzo[d]oxazol-2-yl)-N-(2-methoxyethyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1142**);
6-(4-(hydroxymethyl)-5-isopropyloxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1143**);
6-(6-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1145**);
2-((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)acetic acid (**C1146**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboxamide (**C1149**);

6-(4-methoxybenzo[d]oxazol-2-yl)-5-((2-methoxyethoxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1151**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((oxetan-3-yloxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1152**);
6-(5-isopropyl-4-(methoxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1153**);
6-(7-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1154**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboxylic acid (**C1155**);
6-(6-aminobenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1156**);
6-(5-cyclohexyl-4-(hydroxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1157**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(((2-oxopyrrolidin-3-yl)oxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1159**);
6-(6-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1160**);
6-(4-methoxy-6-(methylamino)benzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1161**);
6-(6-(dimethylamino)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1162**);
4-methoxy-N,N,N-trimethyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-6-aminium (**C1163**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazole-4-carboxylic acid (**C1165**);
6-(6-(hydroxymethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1166**);
6-(4-methoxyoxazolo[4,5-c]pyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1167**);
5-cyclohexyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazole-4-carboxylic acid (**C1169**);

5-methyl-6-(oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1170**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-(m-tolyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1172**);
3-(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)propanoic acid (**C1173**);
6-(5-amino-7-methoxyoxazolo[5,4-d]pyrimidin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1174**);
6-(6-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1175**);
5-(((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)methyl)oxazolidin-2-one (**C1177**);
N-(2-hydroxyethyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1178**);
5-((1H-imidazol-1-yl)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1180**);
6-(5-aminobenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1181**);
5-(((1H-imidazol-5-yl)methoxy)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1182**);
5-ethyl-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1183**);
(R)-6-(4-(methoxymethyl)-4,5-dihydrooxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1184**);
6-(4-methoxybenzo[d]oxazol-2-yl)-N-(oxetan-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1185**);
methyl (S)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylate (**C1187**);
6-(4-ethylbenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1188**);
(S)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1192**);

6-(6-aminobenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1193**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-N-(tetrahydro-2H-pyran-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1194**);
(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carbonyl)glycine (**C1195**);
(S)-N-(1-hydroxypropan-2-yl)-6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1196**);
2-((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)acetamide (**C1198**);
6-(6-amino-7-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1202**);
6-(6-(hydroxymethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1203**);
5-methyl-6-(4-(methylthio)benzo[d]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1204**);
6-(7-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1205**);
6-(5-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1206**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-N-(3,3,3-trifluoro-2-hydroxypropyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1209**);
2-acetyl-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1210**);
2-ethynyl-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1211**);
(4*R*,5*S*)-5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1213**);
(5*S*)-5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1216**);
6-(6-amino-4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1218**);

N-(2-hydroxy-2-methylpropyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1219**);
6-(benzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1222**);
6-(4-aminobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1223**);
6-(7-(hydroxymethyl)-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1224**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(((1-methyl-2-oxopyrrolidin-3-yl)oxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1225**);
5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1226**);
6-(6-amino-4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1227**);
6-(7-aminobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1230**);
5-((2,2-difluoroethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1232**);
ethyl 4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohex-3-ene-1-carboxylate (**C1233**);
4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohex-3-ene-1-carboxylic acid (**C1234**);
5-(3-(hydroxymethyl)cyclopentyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1236**);
3-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclopentane-1-carboxylic acid (**C1239**);
6-(6-(1-hydroxyethyl)-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1240**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-vinylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1241**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-((2-methoxyethoxy)methyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1243**);

6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-*N*-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1244**);
N-((1*H*-pyrazol-3-yl)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1245**);
5-(methoxymethyl)-6-(4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1246**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2(3*H*)-one (**C1247**);
5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1248**);
2-cyano-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxylic acid (**C1249**);
6-(5-amino-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1250**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-5-(((2-oxooxazolidin-5-yl)methoxy)methyl)-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1251**);
3-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclobutane-1-carboxylic acid (**C1252**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(3-methylisoxazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1253**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-5-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4*H*)-one (**C1254**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1255**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-*N*-(1-methyl-1*H*-pyrazol-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1256**);
1-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)piperidine-3-carboxylic acid (**C1257**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-morpholino-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1258**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-((oxetan-3-yloxy)methyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1259**);

5-methyl-6-(oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1270**);
6-(6-amino-7-chlorobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1271**);
6-(4-(dimethylamino)benzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1272**);
5-methyl-7-oxo-3,6-diphenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1273**);
5-methyl-6-(4-(methylamino)benzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1274**);
5-methyl-6-(oxazolo[4,5-*c*]pyridin-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1275**);
6-(1-cyclohexyl-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1276**);
6-(4-cyclopropoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1277**);
5-(dimethylphosphoryl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1284**);
6-(5-cyclopentyl-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1003**);
6-(5-cyclohexyl-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1004**);
6-(5-cyclohexyl-1,3,4-thiadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1006**);
5-methyl-3-phenyl-6-(5-(tetrahydrofuran-2-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1012**);
5-methyl-3-phenyl-6-(5-(pyrrolidin-1-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1014**);
5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-4-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1016**);
6-(5-cyclopentyl-1,3,4-oxadiazol-2-yl)-5-(methoxymethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1018**);

6-(5-(methoxymethyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1019**);
5-methyl-3-phenyl-6-(5-(piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1020**);
6-(5-(3-methoxycyclohexyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (isomers 1 and 2) (**D1021**);
5-methyl-6-(5-(2-methylpyrrolidin-1-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1022**);
5-methyl-6-(5-(1-methylcyclopentyl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1023**);
5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-2-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1024**);
(*S*)-5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1025**);
(*R*)-5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1026**);
6-(5-(3-methoxypiperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1027**);
(*S*)-5-methyl-3-phenyl-6-(5-(2,2,2-trifluoro-1-methoxy-1-phenylethyl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1028**);
(*R*)-5-methyl-3-phenyl-6-(5-(2,2,2-trifluoro-1-methoxy-1-phenylethyl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1029**);
2,5-dimethyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1030**);
5-methyl-6-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1032**);
6-(5-(3-methoxypyrrolidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1037**);
5-methyl-3-phenyl-2-(trifluoromethyl)-6-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1038**);
5-methyl-6-(5-(1-(methylsulfonyl)piperidin-3-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1040**);

6-(5-(2-methoxycyclohexyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (Isomers 1, 2 and 3) (**D1046**);
5-methyl-6-(5-(4-(methylsulfonyl)morpholin-3-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1047**);
6-(5-(2-methoxycyclopentyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (Isomers 1 and 2) (**D1049**);
5-methyl-6-(5-(3-methyltetrahydro-2*H*-pyran-3-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1051**);
6-(5-(1-methoxycyclopentyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1055**);
5-methyl-6-(5-(1-(methylsulfonyl)piperidin-2-yl)-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1056**);
6-(5-(1-acetylpiperidin-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1057**);
6-(5-(1-aminocyclopentyl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1062**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazole-2-carboxamide (**D1066**);
6-(5-(2-hydroxypyridin-3-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1067**);
6-(5-(2-(aminomethyl)piperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1070**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazole-2-carbonitrile (**D1071**);
5-methyl-3-phenyl-6-(5-(1,4,5,6-tetrahydropyrimidin-2-yl)-1,3,4-oxadiazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1072**);
N-(2-(1-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)piperidin-2-yl)ethyl)methanesulfonamide (**D1073**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazole-2-carboximidamide (**D1074**);
1-(5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-1,3,4-oxadiazol-2-yl)guanidine (**D1077**);

6-(5-(4-hydroxypyrimidin-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**D1078**);
6-(5-(3-aminopiperidin-1-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1084**);
6-(5-(2-hydroxypyridin-4-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1085**);
6-(5-(6-hydroxypyridin-2-yl)-1,3,4-oxadiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1086**);
6-(5-cyclohexyl-1,3,4-oxadiazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**D1089**); and
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**E1001**);

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

[00262] In one embodiment, the compound is selected from the group consisting of

N-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1*H*-benzo[*d*]imidazol-7-yl)acetamide (**C1009**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1014**);
6-(5-methoxy-1H-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1016**);
5-methyl-3-phenyl-6-(4,5,6,7-tetrahydro-1H-benzo[*d*]imidazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1017**);
6-(4-methoxy-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1018**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1019**);
6-(7-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1022**);
3-isopropyl-5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2(3*H*)-one (**C1023**);

5-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1024**);
8-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)quinazolin-4(3*H*)-one (**C1025**);
5-methyl-3-phenyl-6-(5-(tetrahydro-2*H*-pyran-3-yl)oxazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1027**);
5-methyl-6-(oxazolo[4,5-b]pyridin-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1030**);
2,5-dimethyl-3-phenyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1032**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-6,7-dihydrobenzo[d]oxazol-4(5*H*)-one (**C1033**);
6-(4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1037**);
6-(4-ethoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1038**);
6-(4-isopropoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1039**);
6-(4-bromobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1040**);
6-(4-(2-methoxyethoxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1041**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-2,5-dimethyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1042**);
6-(8-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1044**);
6-(4-(cyclopropylmethoxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1045**);
6-(4-ethylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1046**);
5-methyl-6-(4-(methylthio)benzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1047**);

6-(4-methoxy-4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1048**);
2-(difluoromethyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1050**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1051**);
6-(4-hydroxy-4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1052**);
6-(4-hydroxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1053**);
6-(4-chlorobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1055**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(methoxymethyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1056**);
6-(5-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1057**);
6-(7-methoxyoxazolo[5,4-*b*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1058**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-5,6,7,8-tetrahydro-4*H*-oxazolo[4,5-*c*]azepin-4-one (**C1059**);
5-methyl-6-(4-methylbenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1060**);
N-(2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl)oxy)ethyl)acetamide (**C1062**);
N-(2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl)oxy)ethyl)methanesulfonamide (**C1066**);
6-(4-methoxybenzo[*d*]thiazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1070**);
5-chloro-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1071**);
6-(4-(benzyloxy)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1073**);

2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazole-4-carbonitrile (**C1075**);
6-(4-fluorobenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1076**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2,5-bis(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1077**);
6-(4-(dimethylamino)benzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1078**);
6-(7-bromo-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1081**);
6-(5-bromo-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1082**);
5-methoxy-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1084**);
5-amino-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1085**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazol-4-yl dimethylcarbamate (**C1088**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carbonitrile (**C1089**);
3-(2-fluorophenyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1091**);
6-(4-methoxy-7-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1092**);
6-(4-methoxy-5-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1093**);
6-(7-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1094**);
6-(5-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1095**);
6-(7-methoxyoxazolo[5,4-*c*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1096**);

5-methyl-6-(4-(methylsulfinyl)benzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1097**);
6-(4-methoxy-6-methylbenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1098**);
5-((benzyloxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1099**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)benzo[*d*]oxazole-7-carbonitrile (**C1100**);
ethyl 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazole-4-carboxylate (**C1101**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazole-4-carboxamide (**C1102**);
5-(hydroxymethyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1103**);
6-(4-(hydroxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1104**);
6-(6-chloro-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1105**);
5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)oxazolo[4,5-*c*]pyridin-4(5*H*)-one (**C1106**);
6-(4-(methoxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1108**);
5-((dimethylamino)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1109**);
6-(7-acetyl-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1111**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-7-carboxamide (**C1113**);
3-(3-fluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1114**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazolo[4,5-c]pyridin-4(5H)-one (**C1116**);

2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-4-yl)oxy)acetic acid (**C1117**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-5-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1118**);
3-(3,5-difluorophenyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1119**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(methylthio)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1121**);
2-((2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-4-yl)oxy)acetamide (**C1122**);
6-(6-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1123**);
6-(4-methoxy-7-(methylsulfonyl)benzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1125**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-5-carbonitrile (**C1126**);
6-(6-(aminomethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1128**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid (**C1130**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid (**C1131**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1132**);
6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-5-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1134**);
6-(6-(aminomethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (HCl salt) (**C1135**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylthio)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1136**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylsulfinyl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1137**);

6-(4-methoxybenzo[d]oxazol-2-yl)-5-((methylsulfonyl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1138**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1139**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboximidamide (**C1141**);
6-(4-methoxybenzo[d]oxazol-2-yl)-N-(2-methoxyethyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1142**);
6-(4-(hydroxymethyl)-5-isopropyloxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1143**);
6-(6-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1145**);
2-((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)acetic acid (**C1146**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboxamide (**C1149**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((2-methoxyethoxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1151**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-((oxetan-3-yloxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1152**);
6-(5-isopropyl-4-(methoxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1153**);
6-(7-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1154**);
4-methoxy-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazole-6-carboxylic acid (**C1155**);
6-(6-aminobenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1156**);
6-(5-cyclohexyl-4-(hydroxymethyl)oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1157**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-(((2-oxopyrrolidin-3-yl)oxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1159**);

6-(6-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1160**);
6-(4-methoxy-6-(methylamino)benzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1161**);
6-(6-(dimethylamino)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1162**);
4-methoxy-N,N,N-trimethyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)benzo[d]oxazol-6-aminium (**C1163**);
2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazole-4-carboxylic acid (**C1165**);
6-(6-(hydroxymethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1166**);
6-(4-methoxyoxazolo[4,5-c]pyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1167**);
5-cyclohexyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)oxazole-4-carboxylic acid (**C1169**);
5-methyl-6-(oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1170**);
6-(4-methoxybenzo[d]oxazol-2-yl)-5-methyl-3-(m-tolyl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1172**);
3-(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)propanoic acid (**C1173**);
6-(5-amino-7-methoxyoxazolo[5,4-d]pyrimidin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1174**);
6-(6-amino-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1175**);
5-(((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)methyl)oxazolidin-2-one (**C1177**);
N-(2-hydroxyethyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1178**);
5-((1H-imidazol-1-yl)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1180**);

6-(5-aminobenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1181**);
5-(((1H-imidazol-5-yl)methoxy)methyl)-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1182**);
5-ethyl-6-(4-methoxybenzo[d]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1183**);
(R)-6-(4-(methoxymethyl)-4,5-dihydrooxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**C1184**);
6-(4-methoxybenzo[d]oxazol-2-yl)-N-(oxetan-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1185**);
methyl (S)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylate (**C1187**);
6-(4-ethylbenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1188**);
(S)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1192**);
6-(6-aminobenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1193**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-N-(tetrahydro-2H-pyran-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1194**);
(6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carbonyl)glycine (**C1195**);
(S)-N-(1-hydroxypropan-2-yl)-6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1196**);
2-((6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidin-5-yl)methoxy)acetamide (**C1198**);
6-(6-amino-7-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1202**);
6-(6-(hydroxymethyl)-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1203**);
5-methyl-6-(4-(methylthio)benzo[d]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1204**);

6-(7-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1205**);
6-(5-chloro-4-methoxybenzo[d]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-a]pyrimidine-2-carbonitrile (**C1206**);
6-(4-methoxybenzo[d]oxazol-2-yl)-7-oxo-3-phenyl-N-(3,3,3-trifluoro-2-hydroxypropyl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxamide (**C1209**);
2-acetyl-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1210**);
2-ethynyl-6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1211**);
(4*R*,5*S*)-5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1213**);
(5*S*)-5-methyl-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-4,5-dihydrooxazole-4-carboxylic acid (**C1216**);
6-(6-amino-4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1218**);
N-(2-hydroxy-2-methylpropyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1219**);
6-(benzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1222**);
6-(4-aminobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1223**);
6-(7-(hydroxymethyl)-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1224**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(((1-methyl-2-oxopyrrolidin-3-yl)oxy)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1225**);
5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1226**);
6-(6-amino-4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-5-(methoxymethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1227**);
6-(7-aminobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1230**);

5-((2,2-difluoroethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1232**);
ethyl 4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohex-3-ene-1-carboxylate (**C1233**);
4-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclohex-3-ene-1-carboxylic acid (**C1234**);
5-(3-(hydroxymethyl)cyclopentyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1236**);
3-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclopentane-1-carboxylic acid (**C1239**);
6-(6-(1-hydroxyethyl)-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1240**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-vinylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1241**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-((2-methoxyethoxy)methyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1243**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-*N*-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1244**);
N-((1*H*-pyrazol-3-yl)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1245**);
5-(methoxymethyl)-6-(4-methoxyoxazolo[4,5-*c*]pyridin-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1246**);
5-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)-1,3,4-oxadiazol-2(3*H*)-one (**C1247**);
5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1248**);
2-cyano-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxylic acid (**C1249**);
6-(5-amino-4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1250**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-5-(((2-oxooxazolidin-5-yl)methoxy)methyl)-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1251**);

3-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)cyclobutane-1-carboxylic acid (**C1252**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(3-methylisoxazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1253**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-5-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4*H*)-one (**C1254**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1255**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-*N*-(1-methyl-1*H*-pyrazol-3-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1256**);
1-(6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-5-yl)piperidine-3-carboxylic acid (**C1257**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-morpholino-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1258**);
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-((oxetan-3-yloxy)methyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1259**);
5-methyl-6-(oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1270**);
6-(6-amino-7-chlorobenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1271**);
6-(4-(dimethylamino)benzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1272**);
5-methyl-7-oxo-3,6-diphenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1273**);
5-methyl-6-(4-(methylamino)benzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1274**);
5-methyl-6-(oxazolo[4,5-*c*]pyridin-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1275**);
6-(1-cyclohexyl-1*H*-benzo[*d*]imidazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1276**);
6-(4-cyclopropoxybenzo[*d*]oxazol-2-yl)-5-methyl-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1277**);

5-(dimethylphosphoryl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1284**); and
6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**E1001**);

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

[00263] As used herein, "alkyl", "C_1, C_2, C_3, C_4, C_5 or C_6 alkyl" or "C_{1-6} alkyl" is intended to include C_1, C_2, C_3, C_4, C_5 or C_6 straight chain (linear) saturated aliphatic hydrocarbon groups and C_3, C_4, C_5 or C_6 branched saturated aliphatic hydrocarbon groups. For example, C_1-C_6 alkyl is intended to include C_1, C_2, C_3, C_4, C_5 and C_6 alkyl groups. Examples of alkyl include, moieties having from one to six carbon atoms, such as, but not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl or n-hexyl. The term C_{m-n} means the alkyl group has "m" to "n" carbon atoms. The term "alkylene" refers to an alkyl group having a substituent, i.e. as used here in it is a bivalent alkyl moiety. For example C_{0-3}alkylene, as used herein as part of a substituent of another group includes a direct bond, a linear group -CH_2-, -CH_2CH_2-, or -$CH_2CH_2CH_2$-, or a branched group -$CH(CH_3)$-, -$CH_2CH(CH_3)$-, or -$CH(CH_3)CH_2$-, where C_2 or C_3 alkylene is preferably linear. For groups described as having more than one alkyl component, for example -$N(C_{1-3}alkyl)_2$, -$C(=O)N(C_{1-3}alkyl)_2$, -$P(=O)(C_{1-3}alkyl)_2$, or the like, the alkyl components may be the same or different. For example dialkylamino representes as -$N(C_{1-3}alkyl)_2$ includes *N*,*N*-dimethylamino, *N*,*N*-diethylamino, *N*-isopropyl-*N*-methyl-amino, and the like.

[00264] In certain embodiments, a straight chain or branched alkyl has six or fewer carbon atoms (*e.g.*, C_1-C_6 for straight chain, C_3-C_6 for branched chain), and in another embodiment, a straight chain or branched alkyl has four or fewer carbon atoms.

[00265] As used herein, the term "cycloalkyl" refers to a saturated or unsaturated nonaromatic hydrocarbon mono-or multi-ring (*e.g.*, fused, bridged, or spiro rings) system having 3 to 30 carbon atoms (*e.g.*, C_{3-10}). For example, a C_{3-8} cycloalkyl is intended to include a monocyclic, bicyclic or tricyclic ring having 3, 4, 5, 6, 7, or 8 carbon atoms. Examples of cycloalkyl rings include, but are not limited to, cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cycloheptenyl, cycloheptyl, cycloheptenyl, adamantyl, cyclooctyl, cyclooctenyl, cyclooctadienyl, fluorenyl, phenyl, naphthyl, indanyl, adamantyl and tetrahydronaphthyl. Bridged rings are also included in the definition of cycloalkyl, including, for example, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane and [2.2.2]bicyclooctane. A bridged ring occurs when one or more

carbon atoms link two non-adjacent carbon atoms. In one embodiment, bridge rings are one or two carbon atoms. It is noted that a bridge always converts a monocyclic ring into a tricyclic ring. When a ring is bridged, the substituents recited for the ring may also be present on the bridge. Fused (*e.g.*, naphthyl, tetrahydronaphthyl) and spiro rings are also included. In the case of multicyclic rings, none of the rings is aromatic.

[00266] The term "heterocycloalkyl" refers to a saturated or unsaturated nonaromatic 3-8 membered monocyclic, 7-12 membered bicyclic (fused, bridged, or spiro rings), or 11-14 membered tricyclic ring system (fused, bridged, or spiro rings) having one or more heteroatoms (such as O, N, S, or Se), unless specified otherwise. For example, a 3 to 12-membered heterocycloalkyl ring is intended to include a monocyclic, bicyclic, or tricyclic ring having 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 atoms selected from C, O, N, S, and Se. In the case of multicyclic rings, none of the rings is aromatic. Examples of heterocycloalkyl groups include, but are not limited to, piperidinyl, piperazinyl, pyrrolidinyl, dioxanyl, tetrahydrofuranyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, oxiranyl, azetidinyl, oxetanyl, thietanyl, 1,2,3,6-tetrahydropyridinyl, tetrahydropyranyl, dihydropyranyl, pyranyl, morpholinyl, 1,4-diazepanyl, 1,4-oxazepanyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 2,5-diazabicyclo[2.2.1]heptanyl, 2-oxa-6-azaspiro[3.3]heptanyl, 2,6-diazaspiro[3.3]heptanyl, 1,4-dioxa-8-azaspiro[4.5]decanyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, imidazolinyl, morpholinyl, octahydroisoquinolinyl, oxazolinyl (dihydrooxazolyl), oxazolidinyl, piperidonyl, 4-piperidonyl, piperonyl, pyranyl, pyrazolidinyl, pyrazolinyl, pyrrolinyl, 2H-pyrrolyl, quinuclidinyl, 6*H*-1,2,5-thiadiazinyl, and the like.

[00267] Substituted alkyl is alkyl in which the designated substituents replace one or more hydrogen atoms on one or more carbons of the hydrocarbon backbone. Such substituents can include, for example, alkyl, alkenyl, alkynyl, halogen, hydroxyl, oxo, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

[00268] An "arylalkyl" or an "aralkyl" moiety is an alkyl substituted with an aryl (*e.g.*, phenylmethyl (benzyl)). An "alkylaryl" moiety is an aryl substituted with an alkyl (*e.g.*, methylphenyl).

[00269] As used herein, "alkylene linker" is intended to include C_1, C_2, C_3, C_4, C_5 or C_6 straight chain (linear) saturated divalent aliphatic hydrocarbon groups and C_2, C_3, C_4, C_5 or C_6 branched saturated aliphatic hydrocarbon groups. For example, C_{1-3} alkylene linker as used in describing Q^1 and Q^2 of Formula I herein is a C_{1-3} alkylene intended to include C_1, C_2, and C_3 alkyl linker groups. These linker groups bind to the core Formula I and to T^1 or T^2. Examples of alkylene linker include, moieties having from one to six carbon atoms, such as, but not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, i-butyl, n-pentyl, s-pentyl, or n-hexyl.

[00270] "Alkenyl" includes unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but that contain at least one double bond. For example, the term "alkenyl" includes straight chain alkenyl groups (*e.g.*, ethenyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, decenyl), and branched alkenyl groups. In certain embodiments, a straight chain or branched alkenyl group has six or fewer carbon atoms in its backbone (*e.g.*, C_2-C_6 for straight chain, C_3-C_6 for branched chain). The term "C_{2-6}" or "C_2-C_6" includes alkenyl groups containing two to six carbon atoms. The term "C_{3-6}" or "C_3-C_6" includes alkenyl groups containing three to six carbon atoms.

[00271] Substituted alkenyl is alkenyl in which the designated substituents replace one or more hydrogen atoms on one or more hydrocarbon backbone carbon atoms. Such substituents can include, for example, alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

[00272] "Alkynyl" includes unsaturated aliphatic groups analogous in length and possible substitution to the alkyl groups described above, but which contain at least one triple bond. For example, "alkynyl" includes straight chain alkynyl groups (*e.g.*, ethynyl, propynyl,

butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, decynyl), and branched alkynyl groups. In certain embodiments, a straight chain or branched alkynyl group has six or fewer carbon atoms in its backbone (*e.g.*, C_2-C_6 for straight chain, C_3-C_6 for branched chain). The term "C_{2-6}" or "C_2-C_6" includes alkynyl groups containing two to six carbon atoms. The term "C_{3-6}" or "C_3-C_6" includes alkynyl groups containing three to six carbon atoms.

[00273] Substituted alkynyl is alkynyl in which the designated substituents replace one or more hydrogen atoms on one or more hydrocarbon backbone carbon atoms. Such substituents can include, for example, alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

[00274] Other optionally substituted moieties (such as optionally substituted cycloalkyl, heterocycloalkyl, aryl, or heteroaryl) include both the unsubstituted moieties and the moieties having one or more of the designated substituents. For example, substituted heterocycloalkyl includes those substituted with one or more alkyl groups, such as 2,2,6,6-tetramethyl-piperidinyl and 2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridinyl.

[00275] "Aryl" includes groups with aromaticity, including "conjugated," or multicyclic systems with at least one aromatic ring and lacking a heteroatom in the ring structure. For example, a C_{6-10}aryl is intended to include a monocyclic, bicyclic or tricyclic ring having 6, 7, 8, 9, or 10 carbon atoms. Examples include phenyl, 1,2,3,4-tetrahydronaphthalenyl, naphthalene, etc.

[00276] "Heteroaryl" groups are aryl groups, as defined above, except having from one to four heteroatoms in the ring structure, and may also be referred to as "aryl heterocycles" or "heteroaromatics." For example, a 5 to 10-membered heteroaryl ring is intended to include a stable 5-, 6-, 7-, 8-, or 9-membered monocyclic or 5-, 6-, 7-, 8-, 9-, or 10-membered bicyclic aromatic heterocyclic ring which consists of carbon atoms and one or more heteroatoms, *e.g.*, 1 or 1-2 or 1-3 or 1-4 or 1-5 or 1-6 heteroatoms, or *e.g.*,1, 2, 3, 4, 5, or 6 heteroatoms, independently selected from the group consisting of nitrogen, oxygen, sulfur, selenium, and boron. The nitrogen atom may be substituted or unsubstituted (*i.e.*, N or NR wherein R is H

or other substituents, as defined). The nitrogen and sulfur heteroatoms may optionally be oxidized (*i.e.*, N→O and $S(=O)_p$, where p = 1 or 2). It is to be noted that total number of S and O atoms in the aromatic heterocycle is not more than 1. Preferred heteroaryl groups herein include 5- or 6-membered monocyclic heteroaryl or 9- or 10-membered bicyclic heteroaryl.

[00277] Examples of heteroaryl groups include pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolinyl, indolyl, 3H-indolyl, isoindolyl, isoquinolinyl, pyridazinyl, pyridooxazolyl, pyridoimidazolyl, pyridothiazoyle, pyridinyl, pyrimidinyl, oxadiazolyl (e.g. 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl), pyrazolopyridinyl, benzimidazolyl, tetrahydrobenzimidazolyl, benzothiazolyl, benzofuranyl, dihydrobenzofuranyl, pteridinyl, purinyl, pyrazinyl, benzothiofuranyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzothiophenyl, benzoxazolyl, azabenzimidazolyl, azabenzoxazolyl, azabenzothiazolyl, thiadiazolyl (e.g. 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-thiadiazolyl), triazinyl, triazolyl (e.g. 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl), , benzoxazolinyl, benzimidazolinyl, indolizinyl, quinazolinyl, 4*H*-quinolizinyl, quinoxalinyl, benzodioxolyl, benzoxazolyl, benzoxadiazolyl, tetrahydrobenzoxazolyl (e.g. 4,5,6,7-tetrahydrobenzo[*d*]oxazolyl), tetrahydrobenzimidazolyl (e.g. 4,5,6,7-tetrahydro-1*H*-benzo[*d*]imidazolyl), quinolinyl, isoquinolinyl, tetrahydroquinolinyl (e.g. 1,2,3,4-tetrahydroquinolinyl), tetrahydroisoquinolinyl (e.g. 1,2,3,4-tetrahydroisoquinolinyl), naphthrydinyl, deazapurinyl, benzodihydropyranyl, imidazopyridinyl (e.g. imidazo[1,2-*a*]]pyridinyl), indazolyl, pyrazolopyrimidinyl (e.g. pyrazolo[1,5-*a*]pyrimidinyl), 5,6,7,8-tetrahydro-4H-cyclohepta[d]oxazolyl, oxazolopyrimidinyl (e.g. oxazolo[5,4-*d*]pyrimidinyl), oxazolopyridinyl (e.g. oxazolo[4,5-*b*]pyridinyl, oxazolo[5,4-*b*]pyridinyl, oxazolo[5,4-*c*]pyridinyl, oxazolo[4,5-*c*]pyridinyl), isobenzofuranyl, dihydroisobenzofuranyl, triazolopyridinyl, tetrahydrooxazoloazepinyl (e.g. 5,6,7,8-tetrahydro-4H-oxazolo[4,5-c]azepinyl), azocinyl, carbazolyl, 4a*H*-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, isoindolinyl, indolenyl, isatinonyl, isochromanyl, isoindazolyl, naphthyridinyl, thianthrenyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, xanthenyl, furazanyl, oxindolyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathinyl, phenoxazineyl, phthalazinyl, and the like.

[00278] Furthermore, the terms "aryl" and "heteroaryl" include multicyclic aryl and heteroaryl groups, *e.g.*, tricyclic or bicyclic rings.

[00279] In the case of multicyclic aromatic rings, only one of the rings needs to be aromatic (*e.g.*, 2,3-dihydroindole), although all of the rings may be aromatic (*e.g.*, quinoline). The second ring can also be fused or bridged.

[00280] The cycloalkyl, heterocycloalkyl, aryl, or heteroaryl ring can be substituted at one or more ring positions (*e.g.*, the ring-forming carbon or heteroatom such as N) with such substituents as described above, for example, alkyl, alkenyl, alkynyl, halogen, hydroxyl, oxo, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminocarbonyl, aralkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety. Aryl and heteroaryl groups can also be fused or bridged with alicyclic or heterocyclic rings, which are not aromatic so as to form a multicyclic system (*e.g.*, tetralin, methylenedioxyphenyl).

[00281] The term "substituted," as used herein, means that any one or more hydrogen atoms on the designated atom is replaced with a selection from the indicated groups, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. . When a moiety is indicated as substituted with one or more substituents, this typically indicates substitution with 1, 2, 3, 4, 5, or more, including 1 to 5, 1 to 4, 1 to 3, 1 to 2 or 1 substituents independently selected from an indicated group. When a substituent is oxo or keto (*i.e.*, =O), then 2 hydrogen atoms on the atom are replaced. Keto substituents are not present on aromatic moieties. Ring double bonds, as used herein, are double bonds that are formed between two adjacent ring atoms (*e.g.*, C=C, C=N or N=N). "Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

[00282] When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom in the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound

of a given formula, then such substituent may be bonded via any atom in such formula. Combinations of substituents and/or variables are permissible, but only if such combinations result in stable compounds.

[00283] When any variable (*e.g.*, X^1) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 X^1 moieties, then the group may optionally be substituted with up to two X^1 moieties and X^1 at each occurrence is selected independently from the definition of X^1. Also, combinations of substituents and/or variables are permissible, but only if such combinations result in stable compounds.

[00284] The term "hydroxy" or "hydroxyl" includes groups with an -OH or $-O^-$.

[00285] As used herein, "halo" or "halogen" refers to fluoro, chloro, bromo and iodo. The term "perhalogenated" generally refers to a moiety wherein all hydrogen atoms are replaced by halogen atoms. The term "haloalkyl" or "haloalkoxyl" refers to an alkyl or alkoxyl substituted with one or more halogen atoms. For example, $C_{1\text{-}6}$haloalkyl indicates a 1 to 6 carbon alkyl group (linear or branched) where one or more hydrogens is replaced with a halogen.

[00286] The term "carbonyl" includes compounds and moieties which contain a carbon connected with a double bond to an oxygen atom. Examples of moieties containing a carbonyl include, but are not limited to, aldehydes, ketones, carboxylic acids, amides, esters, anhydrides, etc.

[00287] The term "carboxyl" refers to –COOH or its C_1-C_6 alkyl ester.

[00288] "Acyl" includes moieties that contain the acyl radical (R-C(=O)-) or a carbonyl group. "Substituted acyl" includes acyl groups where one or more of the hydrogen atoms are replaced by, for example, alkyl groups, alkynyl groups, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

[00289] "Alkoxyalkyl," "alkylaminoalkyl," and "thioalkoxyalkyl" include alkyl groups, as described above, wherein oxygen, nitrogen, or sulfur atoms replace one or more hydrocarbon backbone carbon atoms.

[00290] The term "alkoxy" or "alkoxyl" includes substituted and unsubstituted alkyl groups covalently linked to an oxygen atom. Examples of alkoxy groups or alkoxyl radicals include, but are not limited to, methoxy, ethoxy, isopropyloxy, propoxy, butoxy and pentoxy groups. Examples of substituted alkoxy groups include halogenated alkoxy groups. The alkoxy groups can be substituted with groups such as alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moieties. Examples of halogen substituted alkoxy groups include, but are not limited to, fluoromethoxy, difluoromethoxy, trifluoromethoxy, chloromethoxy, dichloromethoxy and trichloromethoxy.

[00291] The term "ester" includes compounds or moieties which contain a carbon or a heteroatom bound to an oxygen atom which is bonded to the carbon of a carbonyl group. The term "ester" includes alkoxycarboxy groups such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, pentoxycarbonyl, etc.

[00292] "Tautomer" is one of two or more structural isomers that exist in equilibrium and is readily converted from one isomeric form to another. This conversion results in the formal migration of a hydrogen atom accompanied by a switch of adjacent conjugated double bonds. Tautomers exist as a mixture of a tautomeric set in solution. In solutions where tautomerization is possible, a chemical equilibrium of the tautomers will be reached. The exact ratio of the tautomers depends on several factors, including temperature, solvent and pH. The concept of tautomers that are interconvertable by tautomerizations is called tautomerism.

[00293] Of the various types of tautomerism that are possible, two are commonly observed. In keto-enol tautomerism a simultaneous shift of electrons and a hydrogen atom occurs. Ring-chain tautomerism arises as a result of the aldehyde group (-CHO) in a sugar chain molecule

reacting with one of the hydroxy groups (-OH) in the same molecule to give it a cyclic (ring-shaped) form as exhibited by glucose.

[00294] Common tautomeric pairs are: ketone-enol, amide-nitrile, lactam-lactim, amide-imidic acid tautomerism in heterocyclic rings (*e.g.*, in nucleobases such as guanine, thymine and cytosine), imine-enamine and enamine-enamine. An example of keto-enol equilibria is between pyrazolo[1,5-a]pyrimidin-7(4H)-ones and the corresponding pyrazolo[1,5-a]pyrimidin-7-ol, as shown below.



pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one pyrazolo[1,5-*a*]pyrimidin-7-ol

[00295] It is to be understood that the compounds of the present invention may be depicted as different tautomers. It should also be understood that when compounds have tautomeric forms, all tautomeric forms are intended to be included in the scope of the present invention, and the naming of the compounds does not exclude any tautomer form. It will be understood that certain tautomers may have a higher level of activity than others.

Synthesis of pyrazolopyrimidinone and triazolopyrimidinone compounds

[00296] The present invention provides methods for the synthesis of the compounds of any Formula disclosed herein. The present invention also provides detailed methods for the synthesis of various disclosed compounds of the present invention according to the following schemes and further exemplified for specific compounds as shown in the Examples.

[00297] Throughout the description, where compositions are described as having, including, or comprising specific components, it is contemplated that compositions also consist essentially of, or consist of, the recited components. Similarly, where methods or processes are described as having, including, or comprising specific process steps, the processes also consist essentially of, or consist of, the recited processing steps. Further, it should be understood that the order of steps or order for performing certain actions is immaterial so long as the invention remains operable. Moreover, two or more steps or actions can be conducted simultaneously.

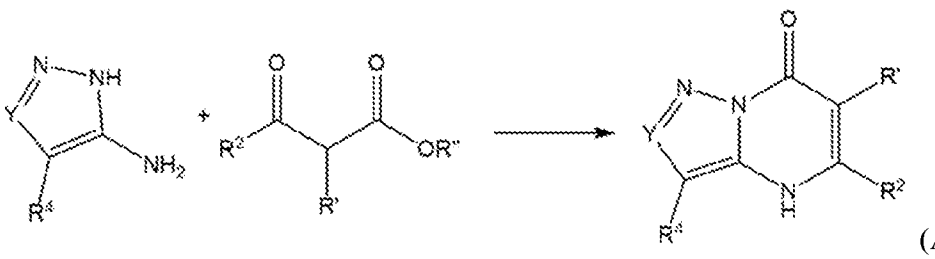
[00298] The synthetic processes of the invention can tolerate a wide variety of functional groups, therefore various substituted starting materials can be used. The processes generally provide the desired final compound at or near the end of the overall process, although it may

be desirable in certain instances to further convert the compound to a pharmaceutically acceptable salt, solvate, hydrate, ester, or prodrug thereof.

[00299] Compounds of the present invention can be prepared in a variety of ways using commercially available starting materials, compounds known in the literature, or from readily prepared intermediates, by employing standard synthetic methods and procedures either known to those skilled in the art, or which will be apparent to the skilled artisan in light of the teachings herein. Standard synthetic methods and procedures for the preparation of organic molecules and functional group transformations and manipulations can be obtained from the relevant scientific literature or from standard textbooks in the field. Although not limited to any one or several sources, classic texts such as Smith, M. B., March, J., *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th edition, John Wiley & Sons: New York, 2001; Greene, T.W., Wuts, P.G. M., *Protective Groups in Organic Synthesis*, 3rd edition, John Wiley & Sons: New York, 1999; R. Larock, *Comprehensive Organic Transformations*, VCH Publishers (1989); L. Fieser and M. Fieser, *Fieser and Fieser's Reagents for Organic Synthesis*, John Wiley and Sons (1994); and L. Paquette, ed., *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons (1995), incorporated by reference herein, are useful and recognized reference textbooks of organic synthesis known to those in the art. The following descriptions of synthetic methods are designed to illustrate, but not to limit, general procedures for the preparation of compounds of the present invention.

[00300] For example, compounds of the present invention can be prepared according to the processes illustrated below in Scheme 1, 2, 3, and 4.

Scheme 1

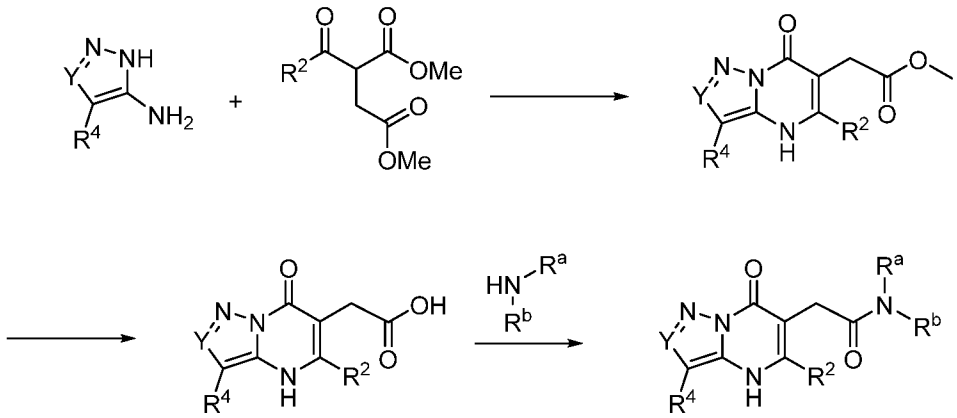


(A)

[00301] Scheme 1 shows the synthesis of a compound of Formala (A), which can be a compound of Formula (I) , where Y can be CR^3 (Formula IA) or Y can be N (Formula IA'), R' is R^1, and R^1, R^2, R^3 and R^4 are within the definitions of Formula I (see e.g. Example 5), or can provide an intermediate that can be further reacted to provide compounds of Formula I (e.g. R' can be -C(=O)OMe, -CH_2C(=O)Me (see Examples 1 or 2), hydrogen (see Example 3

or 12). R'' is e.g. methyl or ethyl. Substituted aminopyrazoles, or aminotriazoles, many of which are commercially available or can be made by reacting a beta-keto amide with an appropriately substituted hydrazide, or by using other chemistry known to one skilled in the art, can be condensed with an appropriately substituted beta-keto ester to give compounds of A, including compounds of Formula (I).

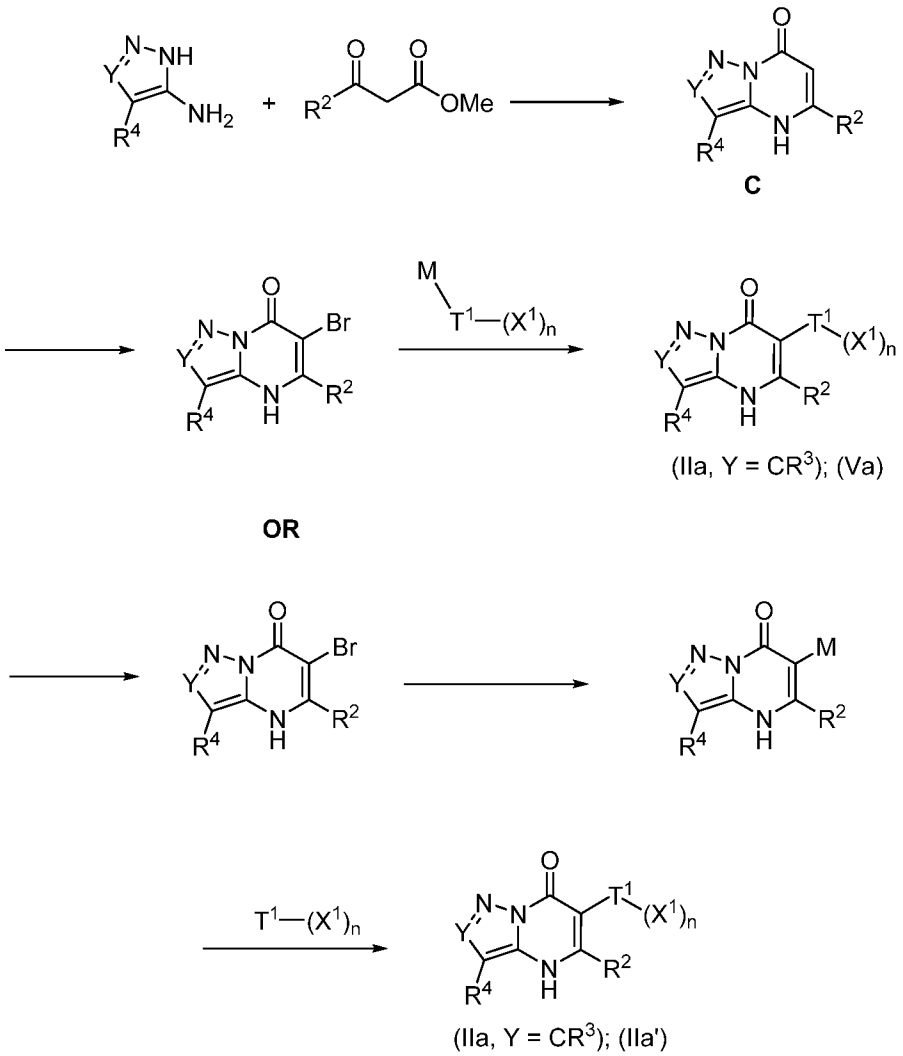
Scheme 2



B (IId, Y = CR^3); (IId')

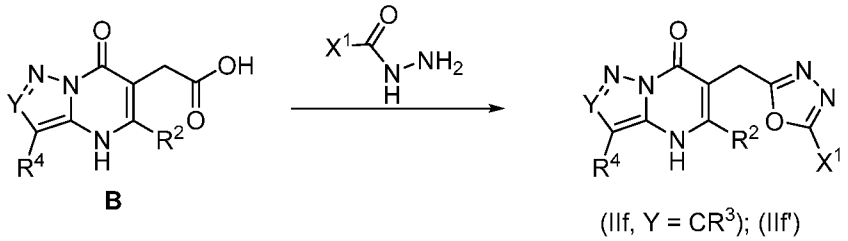
[00302] Scheme 2 shows the synthesis of pyrazolopyrimidinones of Formulas (IId) and triazolopyrimidinones of Formula (IId'), where Y, R^2, R^4, R^a and R^b are within the definitions of Formula (I). An aminopyrazole or amino triazole can be condensed with an appropriate beta-keto ester, *e.g.*, dimethyl 2-acetylsuccinate, to give an ester (e.g. R' of above scheme 1 = $CH_2C(=O)OMe$, see Example 2) that is then saponified to produce an acid (compound B). The acid can then be coupled to an NR^aR^b group to give compounds of Formula (IId) or (IId'). Compounds of Formulas (IIc) or (IIc') can be synthesized using a similar route, starting with a beta-keto ester such as dimethyl 2-acetylmalonate (e.g. scheme 1 where R' = C(=O)OMe, see Example 1).

Scheme 3



[00303] Scheme 3 shows the synthesis of some pyrazolopyrimidinones of Formula (IIa) or triazolopyrimidinones of Formula (IIa'), where Y, R^2, R^4, T^1 and X^1 are within the definitions of Formula (I). An aminopyrazole or aminotriazole can be condensed with an appropriate beta-keto ester to give compound C (e.g. scheme 1 where R' is H) an ester that is subsequently brominated (e.g. per Example 3, the corresponding iodo compound is prepared per Example 4) . The T^1-X^1 group can then be introduced through a metal-catalyzed cross-coupling reaction with an M-T^1-X^1 group to give compounds of Formula (IIa) or (IIa'). Alternatively, the brominated intermediate can be converted to a metalated nucleophile, which can then react with an electrophilic T^1-X^1 group to form compounds of Formula (IIa) or (IIa'). "M" refers to metallic functional groups such as $B(OH)_2$, $Sn(alkyl)_3$, $Si(alkyl)_3$, MgBr, Li, CuLi, ZnCl, and the like. Specific reactions where R' is Br are found in Examples 3 and R' iodo in Examples 4, 10, and 12.

Scheme 4

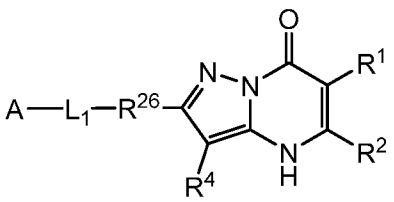


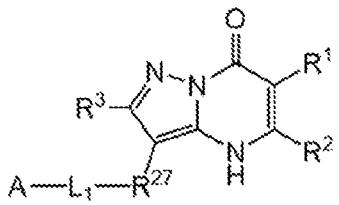
[00304] Scheme 4 shows the synthesis of compounds of Formula (IIf) and (IIf') from acid Compound B (see scheme 2). Compound B can be treated with an appropriate hydrazide, *e.g.*, acetylhydrazide, to give compounds of Formula (IIf) or (IIf') (see Examples 2 and 17). Compounds of Formula (IIe) and (IIe') can be synthesized using a similar route, starting from the acid resulting from the reaction of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine with a beta-keto ester such as dimethyl 2-acetylmalonate (see Example 1 and 17). Additional methods of making compounds of Formual (I) are found in the Examples 1-19 below.

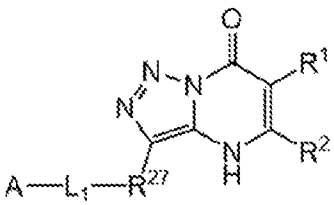
[00305] Compounds of the invention can also be used in the preparation of Proteolysis Targeting Chimeras (PROTACs), wherein the conjugates of the invention are conjugated to ligand that binds an E3 ubiquitin ligase via a suitable linker. For example, a compound of Formula I can be modified off of the R^3 or R^4 substituent position to provide a linker, which can be reacted to bind with a suitable ligand. Thus in one embodiment, a conjugate is provided comprising a compound of the invention that binds cGAS linked to a ligand of an E3 ubiquitin ligase, wherein the resulting conjugate binds to both the E3 ubiquitin ligase and cGAS. This results in the binding of ubiquitin to the cGAS protein by the E3 ubiquitin ligase. The resulting modified cGAS is then processed by the cell, resultling in degradation of the protein. Suitable ligands that bind E3 ubiquitin ligase, and suitable linkers, and methods of making such conjugates are well known to one skilled in the art. See, for example, Collins et al., Biochemical Journal 2017, 474:1127-1147; Bondeson, et al., Nature Chemical Biology 2015, 11:611-617; and Toure and Crews, Angew. Chem. Int. Ed. 2016, 55:2-10.

[00306] Thus, conjugates are provided comprising compounds of the invention linked to a suitable ligand. In one embodiment, compounds of Formula I can be modified by replacing or modifying the R^3 or R^4 substituent, e.g. in compounds of Formula IA, or by replacing or modifying the R^4 substituent in compounds of Formula IA', to provide a suitable substituent comprising a reactive group capable of binding to a suitable linker. In some embodiments, the reactive group comprises a suitable hydroxy or amine group (e.g. an R^3 or R^4 substituent

or modification thereof comprising a terminal -OH, -NH_2, C(=O)NH_2, and the like) that is capable of reacting with a suitable linker. In one embodiment, compounds of Formula I can be modified by replacing or modifying the R^3 or R^4 substituent, e.g. in compounds of Formula IA, or by replacing or modifying the R^4 substituent in compounds of Formula IA', to provide a suitable substituent bound to a linker moiety, wherein said linker moiety comprises a reactive group capable of binding to a suitable ligand. In one embodiment, compounds of Formula I can be modified by replacing or modifying the R^3 or R^4 substituent, e.g. in compounds of Formula IA, or by replacing or modifying the R^4 substituent in compounds of Formula IA', to provide a suitable substituent bound to a linker moiety, wherein said linker moiety is bound to a suitable ligand. In one embodiment, the ligand binds to an E3 ubiquitin ligase. In some embodiments, the E3 ubiquitin ligase is MDM2, cIAP1, CRBN, or VHL. In one embodiment, a modified compound of the invention is a compound of Formula (Va), Formula (Vb), or Formula (Vc):


(Va),


(Vb), or


(Vc),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof. In these formulae, A is an E3 ubiquitin ligase ligand; L_1 is a suitable linker, R^{26} is a suitable R^3 or modification or replacement of R^3 (as defined in Formula I), and R^{27} is a suitable R^4 or modification or replacement of R^4 (as defined in Formula I); and R^1, R^2, R^3, and R^4 are as defined for compounds of Formula (I).

Methods

[00307] The phrase "cGAS/STING pathway-mediated condition," as used herein, comprises autoimmune, inflammatory, and neurodegenerative conditions. For example, the autoimmune disorder is selected from disease can be a type I interferonopathy (e.g., Aicardi-Goutieres Syndrome, Sjögren's syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus,

spondyloenchondrodysplasia), rheumatoid arthritis, juvenile rheumatoid arthritis, idiopathic thrombocytopenic purpura, autoimmune myocarditis, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, psoriasis, Type 1 diabetes, or Type 2 diabetes. For example, the inflammatory disorder is selected from atherosclerosis, dermatomyositis, SIRS, sepsis, septic shock, celiac disease, interstitial cystitis, transplant rejection, inflammatory bowel disease (ulcerative colitis, Crohn's disease), age-related macular degeneration, IgA nephropathy, glomerulonephritis, vasculitis, polymyositis, or Wegener's disease.

[00308] Compound of the invention as described herein, can be useful in treating a variety of diseases, where the modulation of the cGAS/STING pathway can provide therapeutic benefit. In some aspects, a compound of the invention inhibits the cGAS/STING pathway, and can be useful in treating a disease selected from the group consisting of systemic inflammatory response syndrome (SIRS), sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature) syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis, vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease. In some embodiments, compounds of the invention are useful in treating Aicardi-Goutieres Syndrome, X-linked reticulate pigmentary disorder, dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, or Type I or Type II diabetes.

[00309] As used herein, "treating" or "treat" describes the management and care of a mammalian subject (e.g. human patient) for the purpose of combating a disease, condition, or disorder and includes the administration of a compound of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, to alleviate the symptoms or complications of a disease, condition

or disorder, or to eliminate the disease, condition or disorder. The term "treat" can also include treatment of a cell *in vitro* or an animal model.

[00310] A compound of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, can also be used to prevent a disease, condition or disorder, or used to identify suitable candidates for such purposes. As used herein, "preventing" or "prevent" describes reducing or eliminating the onset of the symptoms or complications of the disease, condition or disorder.

[00311] As used herein, the term "alleviate" is meant to describe a process by which the severity of a sign or symptom of a disorder is decreased. Importantly, a sign or symptom can be alleviated without being eliminated. In a preferred embodiment, the administration of pharmaceutical compositions of the invention leads to the elimination of a sign or symptom, however, elimination is not required. Effective dosages are expected to decrease the severity of a sign or symptom. For instance, a sign or symptom of a disorder such as an autoimmune, inflammatory, or neurodegenerative disease, which can occur in multiple locations, is alleviated if the severity of the disease is decreased within at least one of multiple locations.

[00312] Compounds of the present invention can inhibit the cGAS/STING pathway and, accordingly, in one aspect of the invention, certain compounds disclosed herein are candidates for treating, or preventing certain conditions and diseases. The present invention provides methods for treating conditions and diseases wherein the course of the condition or disease can be influenced by the cGAS/STING pathway. The method includes administering to a subject in need of such treatment, a therapeutically effective amount of a compound of the present invention, or a pharmaceutically acceptable salt, metabolite, solvate, hydrate, or stereoisomer thereof.

[00313] The present invention provides a method of inhibiting the cGAS/STING pathway in a cell, comprising contacting the cell with one or more compounds or compositions of the present invention.

[00314] The present invention also provides a method of treating a cGAS/STING pathway-mediated condition, comprising administering to a patient in need thereof an effective amount of one or more compounds or compositions of the present invention. In some embodiments, the cGAS/STING pathway-mediated condition is an autoimmune, inflammatory, or neurodegenerative condition or cancer (see Rayburn, E. R. et al., Mol Cell Pharmacol. 2009; 1(1): 29–43 and Urbanska, A.M. et al., Cell Biochem Biophys. 2015 Jul;72(3):757-69).

[00315] The present invention also provides a method of inhibiting type I interferon production mediated by the cGAS/STING pathway comprising: administering to the subject in need thereof a therapeutically effective amount of one or more compounds or compositions of the present invention. The cGAS/STING pathway of cytosolic DNA sensing as that phrase is used herein comprises the following proteins: SAMHD1, DNase II, STAT1, STAT2, TREX1, ENPP1, cGAS, STING, IRF3, IRF7, TBK1, IKK, and NF-κB. Such a method may be practiced *in vitro*, in a cell, or in an organism (e.g., in a human).

[00316] The present invention also provides a method of treating a type I interferon-mediated disease in a subject, comprising: administering to the subject in need thereof a therapeutically effective amount of one or more compounds or compositions of the present invention.

[00317] The present invention also provides a method of inhibiting cytokine production in a cell, comprising: contacting the cell with one or more compounds or compositions of the present invention.

[00318] The present invention also provides a method of treating a cytokine-mediated disease in a subject, comprising: administering to the subject in need thereof a therapeutically effective amount of one or more compounds or compositions of the present invention.

[00319] The present invention provides a method of treating an autoimmune disease in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of one or more compounds or compositions of the present invention. In some embodiments, the autoimmune disease can be a type I interferonopathy (e.g., Aicardi-Goutieres Syndrome, Sjögren's syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, spondyloenchondrodysplasia), rheumatoid arthritis, juvenile rheumatoid arthritis, idiopathic thrombocytopenic purpura, autoimmune myocarditis, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, psoriasis, Type 1 diabetes, or Type 2 diabetes.

[00320] The present invention provides a method of treating an inflammatory disease in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of one or more compounds or compositions of the present invention. For example, the inflammatory disease can be atherosclerosis, dermatomyositis, SIRS, sepsis, septic shock, celiac disease, interstitial cystitis, transplant rejection, inflammatory bowel disease (ulcerative colitis, Crohn's disease), age-related macular degeneration, IgA nephropathy, glomerulonephritis, vasculitis, polymyositis, or Wegener's disease.

[00321] The present invention further provides a method of treating neurodegenerative diseases in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of one or more compounds or compositions of the present invention. For example, the neurodegenerative disease can be Alzheimer's disease, Parkinson's disease, multiple sclerosis, IgM polyneuropathies, or myasthenia gravis.

[00322] The compounds of the invention can also be use in combination with additional agents for the treatment of autoimmune and inflammatory diseases. Janus Kinase inhibitors (Jak inhibitors) including a Jak1, Jak2, Jak3 or Tyk2 inhibitor, or compound that inhibits any combination thereof, including Jak1/2 inhibitors. Jak inhibitors can block cytokine-mediated signaling via the JAK-STAT pathway, and have been developed for the treatment of a variety of inflammatory and autoimmune diseases. For example, tofacitinib is an approved Jak1 and Jak3 inhibitor used for the treatment of rheumatoid arthritis, psoriatic arthritis and ulcerative colitis; baricitinib is a Jak1 and Jak2 inhibitor approved in Europe, and used in the treatment of rheumatoid arthritis; filgotinib is a Jak1 inhibitor being developed for the treatment of rheumatoid arthritis and Crohn's disease.

[00323] The present invention provides a method of treating a disease in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of a compound of the invention in combination with a Janus Kinase (Jak) inhibitor, including a Jak1, Jak2, Jak3 or Tyk2 inhibitor, or compound that inhibits any combination thereof. In some embodiments, the Jak inhibitor is a Jak1/2 inhibitor. In some embodiments, the Jak inhibitor is selected from the group consisting of ruxolitinib, tofacitinib, oclacitinib, baricitinib, filgotinib, gandotinib, itacitinib, lestaurtinib, momelotinib, pacritinib, upadacitinib, peficitinib, fedratinib, decernotinib, cerdulatinib, tasocitinib, PF-04965842, PF-06651600, PF-06700841, PF-06263276, BMS-986165, BMS-911543, AZD1480, AZD4205, AT9283, CHZ868, and TD-1473. In one embodiment, the disease is selected from the group consisting of SIRS, sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI, CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis,

vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease. In some embodiments, compounds of the invention in combination with a Jak inhibitor are useful in treating Aicardi-Goutieres Syndrome, X-linked reticulate pigmentary disorder, dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, or Type I or Type II diabetes.

[00324] The present invention further provides the use of one or more compounds or compositions of the present invention for inhibiting the cGAS/STING pathway in a cell.

[00325] The present invention further provides the use of one or more compounds or compositions of the present invention for the treatment of a cGAS/STING pathway-mediated condition.

[00326] The present invention further provides the use of one or more compounds or compositions of the present invention for inhibiting type I interferon production mediated by the cGAS/STING pathway in a cell.

[00327] The present invention further provides the use of one or more compounds or compositions of the present invention for the treatment of a type I interferon-mediated disease.

[00328] The present invention further provides the use of one or more compounds or compositions of the present invention for inhibiting cytokine production in a cell.

[00329] The present invention further provides the use of one or more compounds or compositions of the present invention for the treatment of a cGAS/STING pathway-mediated condition.

[00330] The present invention further provides the use of one or more compounds or compositions of the present invention for the treatment of an autoimmune disease. In some embodiments, the autoimmune disease can be a type I interferonopathy (e.g., Aicardi-Goutieres Syndrome, Sjögren's syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, spondyloenchondrodysplasia), rheumatoid arthritis, juvenile rheumatoid arthritis, idiopathic thrombocytopenic purpura, autoimmune myocarditis, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, psoriasis, Type 1 diabetes, or Type 2 diabetes.

[00331] The present invention further provides the use of one or more compounds or compositions of the present invention for the treatment of an inflammatory disease. For example, the inflammatory disease can be atherosclerosis, dermatomyositis, SIRS, sepsis,

septic shock, celiac disease, interstitial cystitis, transplant rejection, inflammatory bowel disease (ulcerative colitis, Crohn's disease), age-related macular degeneration, IgA nephropathy, glomerulonephritis, vasculitis, polymyositis, or Wegener's disease.

[00332] The present invention further provides the use of one or more compounds or compositions of the present invention for the treatment of a neurodegenerative disease. For example, the neurodegenerative disease can be Alzheimer's disease, Parkinson's disease, multiple sclerosis, IgM polyneuropathies, or myasthenia gravis.

[00333] The present invention further provides one or more compounds or compositions of the present invention for use in inhibiting the cGAS/STING pathway in a cell.

[00334] The present invention further provides one or more compounds or compositions of the present invention for use in the treatment of a cGAS/STING pathway-mediated condition.

[00335] The present invention further provides one or more compounds or compositions of the present invention for use in inhibiting type I interferon production mediated by the cGAS/STING pathway in a cell.

[00336] The present invention further provides one or more compounds or compositions of the present invention for use in the treatment of a type I interferon-mediated disease.

[00337] The present invention further provides one or more compounds or compositions of the present invention for use in inhibiting cytokine production in a cell.

[00338] The present invention further provides one or more compounds or compositions of the present invention for use in the treatment of a cGAS/STING pathway-mediated condition.

[00339] The present invention further provides one or more compounds or compositions of the present invention for use in the treatment of an autoimmune disease, such as those described herein.

[00340] The present invention further provides one or more compounds or compositions of the present invention for use in the treatment of an inflammatory disease, such as those described herein.

[00341] The present invention further provides one or more compounds or compositions of the present invention for use in the treatment of a neurodegenerative disease, such as those described herein.

[00342] Any of the one or more compounds or compositions for use described above may be for use in combination with a Janus Kinase (Jak) inhibitor, such as those described herein.

[00343] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for inhibiting the cGAS/STING pathway in a cell.

[00344] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for the treatment of a cGAS/STING pathway-mediated condition.

[00345] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for inhibiting type I interferon production in a cell.

[00346] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for the treatment of a type I interferon-mediated disease.

[00347] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for inhibiting cytokine production in a cell.

[00348] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for the treatment of a cytokine-mediated condition.

[00349] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for the treatment of an autoimmune disease, such as those described herein.

[00350] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for the treatment of an inflammatory disease, such as those described herein.

[00351] The present invention further provides the use of one or more compounds or compositions of the present invention in the manufacture of a medicament for the treatment of a neurodegenerative disease, such as those described herein.

[00352] The present invention further provides the use of one or more compounds or compositions of the present invention in combination with a Janus Kinase (Jak) inhibitor, including a Jak1, Jak2, Jak3 or Tyk2 inhibitor, or compound that inhibits any combination thereof, in the manufacture of a medicament for the treatment of a disease selected from the group consisting of SIRS, sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI, CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative

colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis, vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease. In some embodiments, the Jak inhibitor is a Jak1/2 inhibitor. In some embodiments, the Jak inhibitor is selected from the group consisting of ruxolitinib, tofacitinib, oclacitinib, baricitinib, filgotinib, gandotinib, itacitinib, lestaurtinib, momelotinib, pacritinib, upadacitinib, peficitinib, fedratinib, decernotinib, cerdulatinib, tasocitinib, PF-04965842, PF-06651600, PF-06700841, PF-06263276, BMS-986165, BMS-911543, AZD1480, AZD4205, AT9283, CHZ868, and TD-1473.

[00353] cGAS inhibitory activity of any of the compounds disclosed herein can be determined by reacting the compound in a properly buffered environment with a DNA-activated cGAS in the presence of ATP and GTP. Antagonist activity can then be quantified by measuring the amount of ATP and/or GTP remaining after reaction is halted. Human cGAS sequence encoding amino acids 155-522 (DAAPGASKLRAVLEKLKLSRDDISTAAGMVKGVVDHLLLRLKCDSAFRGVGLLNT GSYYEHVKISAPNEFDVMFKLEVPRIQLEEYSNTRAYYFVKFKRNPKENPLSQFLEGE ILSASKMLSKFRKIIKEEINDIKDTDVIMKRKRGGSPAVTLLISEKISVDITLALESKSS WPASTQEGLRIQNWLSAKVRKQLRLKPFYLVPKHAKEGNGFQEETWRLSFSHIEKEI LNNHGKSKTCCENKEEKCCRKDCLKLMKYLLEQLKERFKDKKHLDKFSSYHVKTA FFHVCTQNPQDSQWDRKDLGLCFDNCVTYFLQCLRTEKLENYFIPEFNLFSSNLIDKR SKEFLTKQIEYERNNEFPVFDEF, SEQ ID No. 1) can be cloned into an expression plasmid to create a construct containing codes for the appropriate proteins and tags (*e.g.*, hexahistidine tag, maltose binding protein fusion, and a cleavable linker) preceding the cGAS sequence. The protein can then be expressed and purified using standard techniques.

[00354] The cGAS/STING pathway inhibitory activity of any of the compounds disclosed herein can also be determined by measuring changes in the type I interferon signature resulting from administration of the compound(s).

[00355] Potential cGAS antagonists, *e.g.*, the pyrazolopyrimidinone compounds disclosed herein, can be made to interact, in a properly buffered environment, with a DNA-activated cGAS in the presence of ATP and GTP. Antagonist activity can then be quantified by measuring the amount of ATP and/or GTP remaining after reaction is halted.

[00356] A cellular assay can be used to assess the compounds of the invention for their ability to inhibit the cGAS/STING pathway. Cells that express a luciferase-based reporter that is linked to IRF-3 activation are used to determine response as a function of compound concentration. Such an assay is described in Vincent et al., Nature Communications 2017, 8(1):750, doi: 10.1038/s41467-017-00833-9.

[00357] A cellular assay can be used to asses the compounds of the invention for their ability to inhibit cytokine production. Bone marrow macrophages harvested from mice can be used to determine response as a function of compound concentration.

Pharmaceutical Compositions

[00358] The present invention also provides pharmaceutical compositions comprising a compound of any Formula disclosed herein in combination with at least one pharmaceutically acceptable excipient or carrier.

[00359] A "pharmaceutical composition" is a formulation containing the compounds of the present invention in a form suitable for administration to a subject. In one embodiment, the pharmaceutical composition is in bulk or in unit dosage form. The unit dosage form is any of a variety of forms, including, for example, a capsule, an IV bag, a tablet, a single pump on an aerosol inhaler or a vial. The quantity of active ingredient (*e.g.*, a formulation of the disclosed compound or salt, hydrate, solvate or isomer thereof) in a unit dose of composition is an effective amount and is varied according to the particular treatment involved. One skilled in the art will appreciate that it is sometimes necessary to make routine variations to the dosage depending on the age and condition of the patient. The dosage will also depend on the route of administration. A variety of routes are contemplated, including oral, pulmonary, rectal, parenteral, transdermal, subcutaneous, intravenous, intramuscular, intraperitoneal, inhalational, buccal, sublingual, intrapleural, intrathecal, intranasal, and the like. Dosage forms for the topical or transdermal administration of a compound of this invention include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. In one embodiment, the active compound is mixed under sterile conditions with a pharmaceutically acceptable carrier, and with any preservatives, buffers, or propellants that are required.

[00360] As used herein, the phrase "pharmaceutically acceptable" refers to those compounds, anions, cations, materials, compositions, carriers, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[00361] "Pharmaceutically acceptable excipient" means an excipient that is useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable, and includes excipient that is acceptable for veterinary use as well as human pharmaceutical use. A "pharmaceutically acceptable excipient" as used in the specification and claims includes both one and more than one such excipient.

[00362] A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical), and transmucosal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

[00363] A compound or pharmaceutical composition of the invention can be administered to a subject in many of the well-known methods currently used for chemotherapeutic treatment. The dose chosen should be sufficient to constitute effective treatment but not so high as to cause unacceptable side effects. The state of the disease condition and the health of the patient should preferably be closely monitored during and for a reasonable period after treatment.

[00364] The term "therapeutically effective amount", as used herein, refers to an amount of a pharmaceutical agent to treat, ameliorate, or prevent an identified disease or condition, or to exhibit a detectable therapeutic or inhibitory effect. The effect can be detected by any assay method known in the art. The precise effective amount for a subject will depend upon the subject's body weight, size, and health; the nature and extent of the condition; and the therapeutic or combination of therapeutics selected for administration. Therapeutically effective amounts for a given situation can be determined by routine experimentation that is within the skill and judgment of the clinician.

[00365]

[00366] For any compound, the therapeutically effective amount can be estimated initially either in cell culture assays, *e.g.*, of neoplastic cells, or in animal models, usually rats, mice, rabbits, dogs, or pigs. The animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans. Therapeutic/prophylactic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, ED_{50} (the dose therapeutically effective in 50% of the population) and LD_{50} (the dose lethal to 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index, and it can be expressed as the ratio, LD_{50}/ED_{50}. Pharmaceutical compositions that exhibit large therapeutic indices are preferred. The dosage may vary within this range depending upon the dosage form employed, sensitivity of the patient, and the route of administration.

[00367] Dosage and administration are adjusted to provide sufficient levels of the active agent(s) or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, general health of the subject, age, weight, and gender of the subject, diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy. Long-acting pharmaceutical compositions may be administered every 3 to 4 days, every week, or once every two weeks depending on half-life and clearance rate of the particular formulation.

[00368] The pharmaceutical compositions containing active compounds of the present invention may be manufactured in a manner that is generally known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes. Pharmaceutical compositions may be formulated in a conventional manner using one or more pharmaceutically acceptable carriers comprising excipients and/or auxiliaries that facilitate processing of the active compounds into preparations that can be used pharmaceutically. Of course, the appropriate formulation is dependent upon the route of administration chosen.

[00369] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under

the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol and sorbitol, and sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[00370] Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[00371] In general, a compound of the application will be administered in therapeutically effective amounts via any of the usual and acceptable modes known in the art, either singly or in combination with one or more therapeutic agents. A therapeutically effective amount may vary widely depending on the severity of the disease, the age and relative health of the subject, the potency of the compound used and other factors. Therapeutic amounts or doses will also vary depending on route of administration, as well as the possibility of co-usage with other agents.

[00372] Upon improvement of a subject's condition, a maintenance dose of a compound, composition or combination of this application may be administered, if necessary. Subsequently, the dosage or frequency of administration, or both, may be reduced, as a function of the symptoms, to a level at which the improved condition is retained when the symptoms have been alleviated to the desired level, treatment should cease. The subject may,

however, require intermittent treatment on a long-term basis upon any recurrence of disease symptoms.

[00373] It will be understood, however, that the total daily usage of the compounds and compositions of the present application will be decided by the attending physician within the scope of sound medical judgment. The specific inhibitory dose for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; the activity of the specific compound employed; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed; and like factors well known in the medical arts.

[00374] The term "pharmaceutical combination" as used herein means a product that results from the mixing or combining of more than one active ingredient and includes both fixed and non-fixed combinations of the active ingredients. The term "fixed combination" means that the active ingredients, *e.g.*, a compound of the application and a co- agent, are both administered to a patient simultaneously in the form of a single entity or dosage. The term "non-fixed combination" means that the active ingredients, *e.g.*, a compound of the application and a co-agent, are both administered to a patient as separate entities either simultaneously, concurrently or sequentially with no specific time limits, wherein such administration provides therapeutically effective levels of the two compounds in the body of the patient. The latter also applies to cocktail therapy, *e.g.*, the administration of three or more active ingredients.

[00375] Oral compositions generally include an inert diluent or an edible pharmaceutically acceptable carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or

Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[00376] For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser, which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

[00377] Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

[00378] The active compounds can be prepared with pharmaceutically acceptable carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Pat. No. 4,522,811.

[00379] It can be advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved.

[00380] In therapeutic applications, the dosages of the pharmaceutical compositions used in accordance with the invention vary depending on the agent, the age, weight, and clinical condition of the recipient patient, and the experience and judgment of the clinician or practitioner administering the therapy, among other factors affecting the selected dosage.

Generally, the dose should be sufficient to result in slowing, and preferably regressing, the progression of the autoimmune, neurodegenerative, or inflammatory disease. Dosages can be in single, divided, or continuous doses (which dose may be adjusted for the patient's weight in kg, body surface area in m^2, and age in years). An effective amount of a pharmaceutical agent is that which provides an objectively identifiable improvement as noted by the clinician or other qualified observer. As used herein, the term "dosage effective manner" refers to amount of an active compound to produce the desired biological effect in a subject or cell.

[00381] The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

[00382] The compounds of the present invention are capable of further forming salts. All of these forms are also contemplated within the scope of the claimed invention.

[00383] As used herein, "pharmaceutically acceptable salts" refer to derivatives of the compounds of the present invention wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines, alkali or organic salts of acidic residues such as carboxylic acids, and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include, but are not limited to, those derived from inorganic and organic acids selected from 2-acetoxybenzoic, 2-hydroxyethane sulfonic, acetic, ascorbic, benzene sulfonic, benzoic, bicarbonic, bisulfate, bitartric, boric, bromic, butyric, calcium, calcium edetic, camsylate, carbonic, chloric, citric, clavularic, dihydrochloric, edetic, ethane disulfonic, 1,2-ethane sulfonic, estolate, esylate, fumaric, glucoheptonic, gluconic, glutamic, glycolic, glycollyarsanilic, hexafluorophosphoric, hexylresorcinic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxymaleic, hydroxynaphthoic, iodic, isethionic, lactic, lactobionic, lauryl sulfonic, maleic, malic, mandelic, methane sulfonic, methylbromic, methylnitric, napsylic, nitric, N-methylglucamine ammonium salt, 3-hydroxy-2-naphthoic, oleic, oxalic, pamoic, pantothenic, phenylacetic, phosphoric, polygalacturonic, propionic, salicyclic, stearic, subacetic, succinic, sulfamic, sulfanilic, sulfuric, sulfosalicylic, suramic, tannic, tartaric, toluene sulfonic, tosyl, triethiodic, trifluoroacetic, and valeric and the commonly occurring amine acids, *e.g.*, glycine, alanine, phenylalanine, arginine, etc.

[00384] In addition to pharmaceutically acceptable salts, the compounds and pharmaceutically acceptable salts as disclosed herein can be "pharmaceutically acceptable solvates", or where

the solvent is water, "pharmaceutically acceptable hydrates". For example, pharmaceutically acceptable solvates may be formed wherein solvent molecules are incorporated into the crystalline lattice during crystallization. Solvates may involve nonaqueous solvents such as ethanol, isopropanol, dimethyl sulfoxide, acetic acid, ethanolamine, and ethyl acetate, or they may involve water as the solvent that is incorporated into the crystalline lattice. Solvates wherein water is the solvent that is incorporated into the crystalline lattice are typically referred to as "hydrates." Hydrates include stoichiometric hydrates as well as compositions containing variable amounts of water. The invention includes all such solvates or hydrates

[00385] When a disclosed compound or its salt is named or depicted by structure, it is to be understood that the compound or salt, including solvates or hydrates thereof, may exist in crystalline forms, non-crystalline forms or a mixture thereof. The compound or salt, or solvates or hydrates thereof, may also exhibit polymorphism (i.e. the capacity to occur in different crystalline forms). These different crystalline forms are typically known as "polymorphs." It is to be understood that when named or depicted by structure, the disclosed compound, or solvates or hydrates thereof, also include all polymorphs thereof. Polymorphs have the same chemical composition but differ in packing, geometrical arrangement, and other descriptive properties of the crystalline solid state. Polymorphs may have different physical properties such as density, shape, hardness, stability, and dissolution properties. Polymorphs typically exhibit different melting points, IR spectra, and X-ray powder diffraction patterns, which may be used for identification. One of ordinary skill in the art will appreciate that different polymorphs may be produced, for example, by changing or adjusting the conditions used during the crystallization or recrystallization of the compounds described herein.

[00386] Other examples of pharmaceutically acceptable salts include hexanoic acid, cyclopentane propionic acid, pyruvic acid, malonic acid, 3-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, 4-methylbicyclo-[2.2.2]-oct-2-ene-1-carboxylic acid, 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, muconic acid, and the like. The present invention also encompasses salts formed when an acidic proton present in the parent compound either is replaced by a metal ion, *e.g.*, an alkali metal ion, an alkaline earth ion, or an aluminum ion; or coordinates with an organic base such as ethanolamine, diethanolamine, triethanolamine, tromethamine, N-methylglucamine, and the like. In the salt form, it is understood that the ratio of the compound to the cation or anion of the salt can be 1:1, or any ration other than 1:1, *e.g.*, 3:1, 2:1, 1:2, or 1:3.

[00387] It should be understood that all references to pharmaceutically acceptable salts include solvent addition forms (solvates) or crystal forms (polymorphs) as defined herein, of the same salt.

[00388] The compounds of the present invention can also be prepared as esters, for example, pharmaceutically acceptable esters. For example, a carboxylic acid function group in a compound can be converted to its corresponding ester, *e.g.*, a methyl, ethyl or other ester. Also, an alcohol group in a compound can be converted to its corresponding ester, *e.g.*, acetate, propionate or other ester.

[00389] The compounds of the present invention can also be prepared as prodrugs, for example, pharmaceutically acceptable prodrugs. The terms "pro-drug" and "prodrug" are used interchangeably herein and refer to any compound which releases an active parent drug *in vivo*. Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (*e.g.*, solubility, bioavailability, manufacturing, etc.), the compounds of the present invention can be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same and compositions containing the same. "Prodrugs" are intended to include any covalently bonded carriers that release an active parent drug of the present invention *in vivo* when such prodrug is administered to a subject. Prodrugs in the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, sulfhydryl, carboxy or carbonyl group is bonded to any group that may be cleaved *in vivo* to form a free hydroxyl, free amino, free sulfhydryl, free carboxy or free carbonyl group, respectively.

[00390] Examples of prodrugs include, but are not limited to, esters (*e.g.*, acetate, dialkylaminoacetates, formates, phosphates, sulfates and benzoate derivatives) and carbamates (*e.g.*, N,N-dimethylaminocarbonyl) of hydroxy functional groups, esters (*e.g.*, ethyl esters, morpholinoethanol esters) of carboxyl functional groups, N-acyl derivatives (*e.g.*, N-acetyl) N-Mannich bases, Schiff bases and enaminones of amino functional groups, oximes, acetals, ketals and enol esters of ketone and aldehyde functional groups in compounds of the invention, and the like, See Bundegaard, H., *Design of Prodrugs*, p1-92, Elesevier, New York-Oxford (1985).

[00391] The compounds, or pharmaceutically acceptable salts, esters or prodrugs thereof, are administered by a route selected from the group consisting of enterally, orally, nasally, transdermally, pulmonary, inhalationally, buccally, sublingually, intraperintoneally,

subcutaneously, intramuscularly, intravenously, rectally, intrapleurally, intrathecally and parenterally. In one embodiment, the compound is administered orally. One skilled in the art will recognize the advantages of certain routes of administration.

[00392] The dosage regimen utilizing the compounds is selected in accordance with a variety of factors including type, species, age, weight, sex and medical condition of the patient; the severity of the condition to be treated; the route of administration; the renal and hepatic function of the patient; and the particular compound or salt thereof employed. An ordinarily skilled physician or veterinarian can readily determine and prescribe the effective amount of the drug required to prevent, counter, or arrest the progress of the condition.

[00393] Techniques for formulation and administration of the disclosed compounds of the invention can be found in *Remington: the Science and Practice of Pharmacy*, 19th edition, Mack Publishing Co., Easton, PA (1995). In an embodiment, the compounds described herein, and the pharmaceutically acceptable salts thereof, are used in pharmaceutical preparations in combination with a pharmaceutically acceptable carrier or diluent. Suitable pharmaceutically acceptable carriers include inert solid fillers or diluents and sterile aqueous or organic solutions. The compounds will be present in such pharmaceutical compositions in amounts sufficient to provide the desired dosage amount in the range described herein.

[00394] All percentages and ratios used herein, unless otherwise indicated, are by weight. Other features and advantages of the present invention are apparent from the different examples. The provided examples illustrate different components and methodology useful in practicing the present invention. The examples do not limit the claimed invention. Based on the present disclosure the skilled artisan can identify and employ other components and methodology useful for practicing the present invention.

[00395] In the synthetic schemes described herein, compounds may be drawn with one particular configuration for simplicity. Such particular configurations are not to be construed as limiting the invention to one or another isomer, tautomer, regioisomer or stereoisomer, nor does it exclude mixtures of isomers, tautomers, regioisomers or stereoisomers; however, it will be understood that a given isomer, tautomer, regioisomer or stereoisomer may have a higher level of activity than another isomer, tautomer, regioisomer or stereoisomer.

[00396] Compounds designed, selected and/or optimized by methods described above, once produced, can be characterized using a variety of assays known to those skilled in the art to determine whether the compounds have biological activity. For example, the molecules can be characterized by conventional assays, including but not limited to those assays described

below, to determine whether they have a predicted activity, binding activity and/or binding specificity.

[00397] Furthermore, high-throughput screening can be used to speed up analysis using such assays. As a result, it can be possible to rapidly screen the molecules described herein for activity, using techniques known in the art. General methodologies for performing high-throughput screening are described, for example, in Devlin (1998) High Throughput Screening, Marcel Dekker; and U.S. Patent No. 5,763,263. High-throughput assays can use one or more different assay techniques including, but not limited to, those described below.

[00398] The present invention provides a kit comprising a compound capable of inhibiting the cGAS/STING pathway selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating an autoimmune disease. In some embodiments, the autoimmune disease can be a type I interferonopathy (e.g., Aicardi-Goutieres Syndrome, Sjögren's syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, spondyloenchondrodysplasia), rheumatoid arthritis, juvenile rheumatoid arthritis, idiopathic thrombocytopenic purpura, autoimmune myocarditis, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, psoriasis, Type 1 diabetes, or Type 2 diabetes.

[00399] The present invention provides a kit comprising a compound capable of inhibiting the cGAS/STING pathway selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating an inflammatory disease. In some embodiments, the inflammatory disease can be atherosclerosis, dermatomyositis, SIRS, sepsis, septic shock, celiac disease, interstitial cystitis, transplant rejection, inflammatory bowel disease (ulcerative colitis, Crohn's disease), age-related macular degeneration, IgA nephropathy, glomerulonephritis, vasculitis, polymyositis, or Wegener's disease.

[00400] The present invention provides a kit comprising a compound capable of inhibiting the cGAS/STING pathway selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating a neurodegenerative disease. In some embodiments, the neurodegenerative disease can be Alzheimer's disease, Parkinson's disease, multiple sclerosis, IgM polyneuropathies, or myasthenia gravis.

[00401] The present invention provides a kit comprising a compound capable of inhibiting type I interferon production selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating an autoimmune disease. In some embodiments, the autoimmune disease can be a type I interferonopathy (e.g., Aicardi-Goutieres Syndrome, Sjögren's syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, spondyloenchondrodysplasia), rheumatoid arthritis, juvenile rheumatoid arthritis, idiopathic thrombocytopenic purpura, autoimmune myocarditis, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, psoriasis, Type 1 diabetes, or Type 2 diabetes.

[00402] The present invention provides a kit comprising a compound capable of inhibiting type I interferon production selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating an inflammatory disease. In some embodiments, the inflammatory disease can be atherosclerosis, dermatomyositis, SIRS, sepsis, septic shock, celiac disease, interstitial cystitis, transplant rejection, inflammatory bowel disease (ulcerative colitis, Crohn's disease), age-related macular degeneration, IgA nephropathy, glomerulonephritis, vasculitis, polymyositis, or Wegener's disease.

[00403] The present invention provides a kit comprising a compound capable of inhibiting type I interferon production selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating a neurodegenerative disease. In some embodiments, the neurodegenerative disease can be Alzheimer's disease, Parkinson's disease, multiple sclerosis, IgM polyneuropathies, or myasthenia gravis.

[00404] The present invention provides a kit comprising a compound capable of inhibiting cytokine production selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating an autoimmune disease. In some embodiments, the autoimmune disease can be a type I interferonopathy (e.g., Aicardi-Goutieres Syndrome, Sjögren's syndrome, Singleton-Merten Syndrome, proteasome-

associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, spondyloenchondrodysplasia), rheumatoid arthritis, juvenile rheumatoid arthritis, idiopathic thrombocytopenic purpura, autoimmune myocarditis, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, psoriasis, Type 1 diabetes, or Type 2 diabetes.

[00405] The present invention provides a kit comprising a compound capable of inhibiting cytokine production selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating an inflammatory disease. In some embodiments, the inflammatory disease can be atherosclerosis, dermatomyositis, SIRS, sepsis, septic shock, celiac disease, interstitial cystitis, transplant rejection, inflammatory bowel disease (ulcerative colitis, Crohn's disease), age-related macular degeneration, IgA nephropathy, glomerulonephritis, vasculitis, polymyositis, or Wegener's disease.

[00406] The present invention provides a kit comprising a compound capable of inhibiting cytokine production selected from one or more compounds of the present invention, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, and instructions for use in treating a neurodegenerative disease. In some embodiments, the neurodegenerative disease can be Alzheimer's disease, Parkinson's disease, multiple sclerosis, IgM polyneuropathies, or myasthenia gravis.

[00407] All publications and patent documents cited herein are incorporated herein by reference as if each such publication or document was specifically and individually indicated to be incorporated herein by reference. Citation of publications and patent documents is not intended as an admission that any is pertinent prior art, nor does it constitute any admission as to the contents or date of the same. The invention having now been described by way of written description, those of skill in the art will recognize that the invention can be practiced in a variety of embodiments and that the foregoing description and examples below are for purposes of illustration and not limitation of the claims that follow.

EXAMPLES

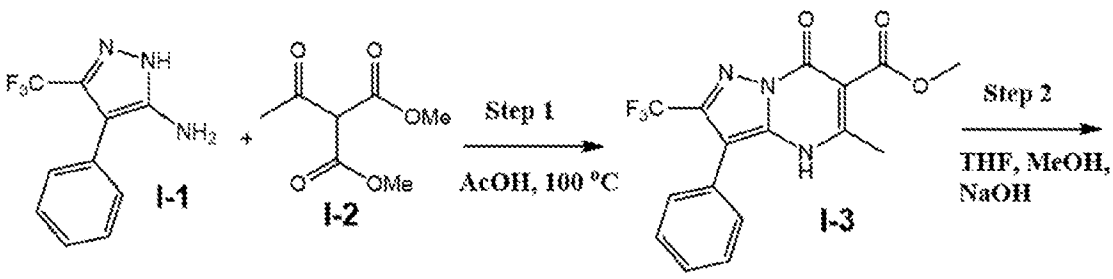
[00408] NMR spectra were recorded on a Bruker Avance II Ultra shield spectrometer (500 MHz). LCMS were acquired on a Waters Alliance 2695 with column heater LC system equipped with a Waters PDA 996 (210-300nm) UV detector and a Waters ZQ 2000, ESI (ES+, 100-1200 amu) MS Detector. Mobile phases (Mobile phase A: Milli-Q H2O + 10mM Ammonium Formate pH: 3.8 (Am.F.), or Ammonium Bicarbonate pH: 10 (Am.B.), Mobile

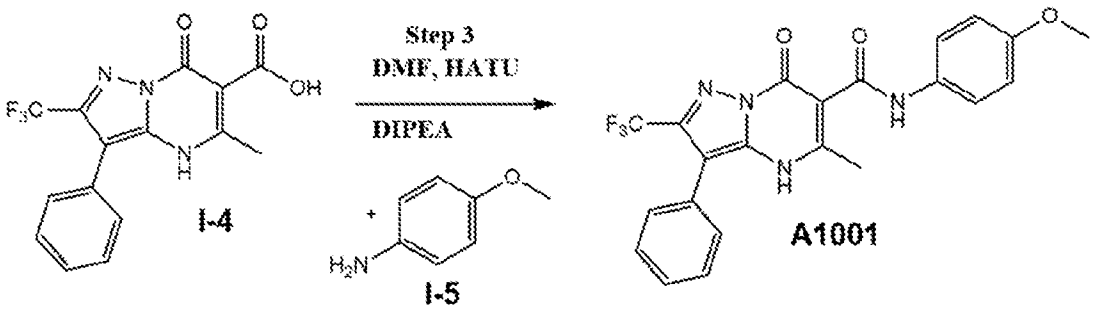
Phase B: CH3CN). LC conditions are: XBridge C18, 3.5µm, 4.6 x 30mm; Iso 5% B for 0.5min, 5% to 100% B in 5 minutes; hold 100% B for 2 minutes; flow rate: 3 mL/min. The methods described in the examples below can be readily modified by one skilled in the art. Compounds made similarly to the exemplified methods may include modifications of reaction conditions, such as any one or more of the reagent concentrations, solvents, reaction times, temperatures, work-up conditions, purification conditions, and the like to provide additional compounds of the invention as described herein.

[00409] Abbreviations and Acronyms. AcOH = acetic acid, Burgess reagent = 1-Methoxy-*N*-triethylammoniosulfonyl-methanimidate, DCM = CH_2Cl_2 = dichloromethane, DIPEA = *N*,*N*-Diisopropylethylamine, DMEDA = *N*,*N'*-Dimethylethylenediamine, DMF = Dimethylformamide, DMSO = Dimethyl sulfoxide, EtOH = ethanol, EtOAc = ethyl acetate, FBS = Fetal Bovine Serum, HATU (Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium) = 1-[Bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxide hexafluorophosphate, LAH = Lithium aluminum hydride, LTB = Lithium tert-butoxide, MeCN = acetonitrile, MeOH = methanol, NaOMe = Sodium methoxide, NBS = *N*-Bromosuccinimide, NIS = *N*-Iodosuccinimide, Pyr-SO_3 = sulfur trioxide pyridine complex, $Pd(dppf)Cl_2$ = [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(ll), TEA = triethylamine, TFA = trifluoroacetic acid, THF = tetrahydrofuran, TEMPO = (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl, $Fe(acac)_3$ = Iron(III) acetylacetonate.

Example 1

[00410] Synthesis of *N*-(4-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1001**) was carried out in three steps as follows:





[00411] Step 1: Synthesis of methyl 5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxylate (**I-3**). To a stirred solution of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine (**I-1**, 2.00 g, 8.80 mmol) (WO 2012149157) in AcOH (10 mL) was added dimethyl 2-acetylmalonate (**I-2**, 1.3 eq, 1.99 g, 11.4 mmol) (JACS, 136(34), 12137-12160, 2014). The reaction mixture was heated at 100 °C for 30 min and concentrated *in vacuo* to dryness. The reaction mixture was triturated in EtOAc for 15 min. The solid was collected by filtration, rinsed with EtOAc, dried under high vacuum to afford the compound **I-3** (1.60 g, 4.55 mmol, 52%) as a white solid which was used without further purification. ^{1}H NMR (500 MHz, DMSO) δ 12.69 (s, 1H), 7.54 – 7.45 (m, 3H), 7.45 – 7.42 (m, 2H), 3.81 (s, 3H), 2.43 (s, 3H); MS (m/z): 325.0 $[M+1]^+$, 97.2%.

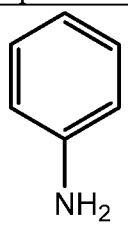
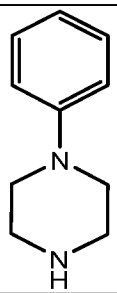
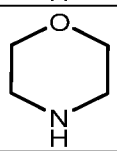
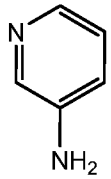
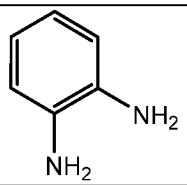
[00412] Step 2: Synthesis of 5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxylic acid (**I-4**). To a stirred solution of compound **I-3** (1.60 g, 4.55 mmol) in a mixture of THF (25 mL) and MeOH (25 mL) was added a solution of sodium hydroxide 2M (18.2 mL, 36.4 mmol). The reaction mixture was stirred at r.t. for 17 h, heated at reflux for 2h and concentrated to dryness. After addition of water and HCl 10%, the white slurry was stirred at r.t. for 10 min. The solid was collected by filtration, rinsed with water, dried under high vacuum to afford compound **I-4** (1.42 g, 4.21 mmol, 92%) as a white solid which was used without further purification. ^{1}H NMR (500 MHz, DMSO) 13.07 (s, 1H), 7.60 – 7.36 (m, 5H), 2.58 (s, 3H); MS (m/z): 337.9 [M+1]+, 96.3%.

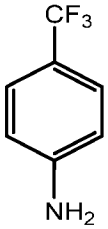
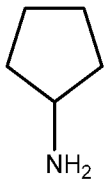
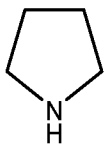
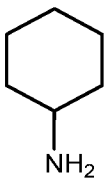
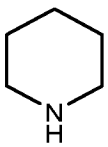
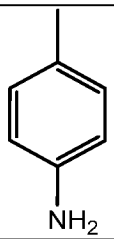
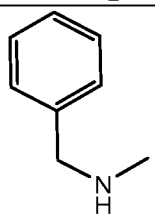
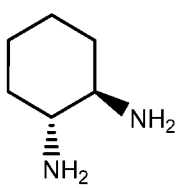
[00413] Step 3: Synthesis of *N*-(4-methoxyphenyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1001**): To a stirred solution of 5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxylic acid (**I-4**, 50 mg, 0.15 mmol) in DMF (1 mL) was added HATU (85 mg, 0.22 mmol), p-anisidine (**I-5**, 27.7 mg, 0.22 mmol) and DIPEA (78 µL, 0.44 mmol). The reaction mixture was stirred at r.t. for 18h. After addition of EtOAc, water and HCl 10%, the layers were separated and the aqueous layer was extracted with EtOAc. The combined organics layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The

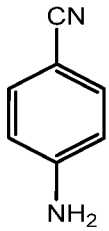
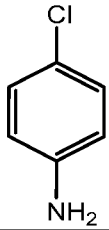
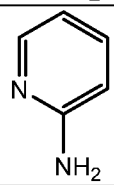
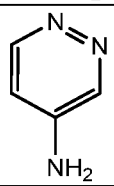
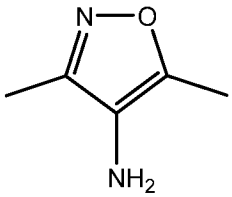
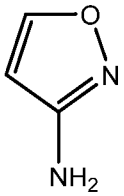
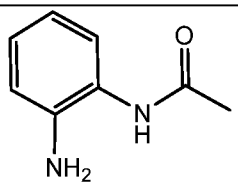
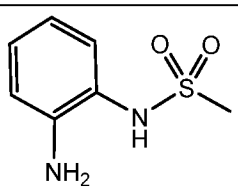
residue was purified by reverse flash chromatography (KP-C18-H5 (Biotage LLC, Charlotte, NC, USA), using a gradient 0 to 100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **A1001** (42 mg, 0.09 mmol, 64%) as a white solid after lyophilization. 1H NMR (500 MHz, DMSO) δ 12.66 (s, 1H), 11.19 (s, 1H), 7.63 – 7.55 (m, 2H), 7.49 (dt, *J* = 15.3, 7.5 Hz, 4H), 7.40 (t, *J* = 7.0Hz, 1H), 6.94 – 6.87 (m, 2H), 3.74 (s, 3H), 2.56 (s, *J* = 12.0Hz, 3H). MS (m/z): 443.1 $[M+1]^+$, >99%.

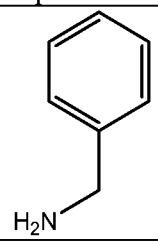
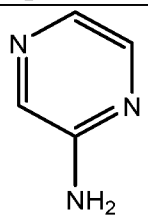
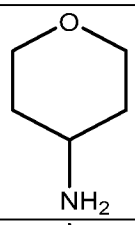
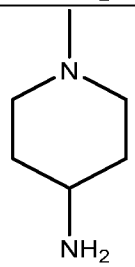
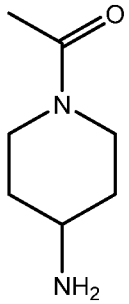
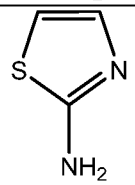
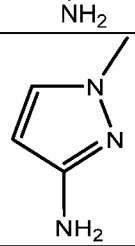
[00414] Table 2 below provides additional compounds that can be synthesized similarly to the methods described in Steps 1-3 above, optionally substituting the listed compound for **I-5**, and/or substituting for **I-1** and/or **I-2** where indicated. Data for compounds synthesized is provided in columns 3-5.

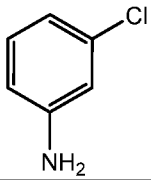
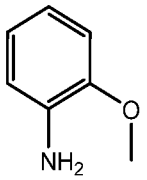
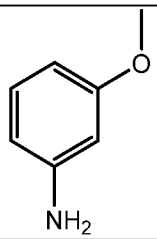
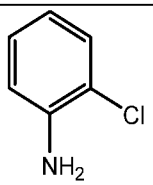
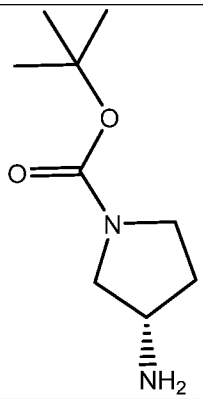
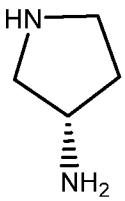
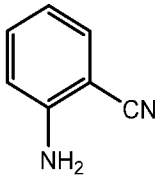
Table 2

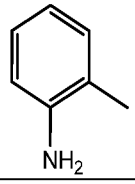
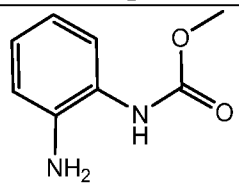
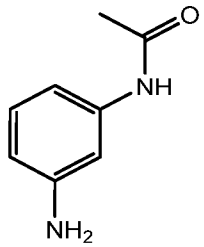
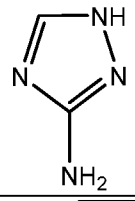
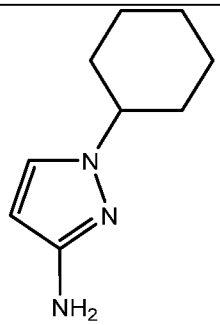
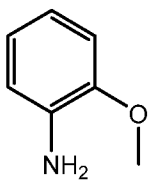
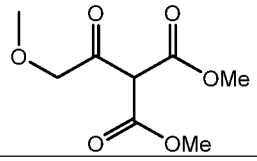
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1002		(500MHz, DMSO) δ 12.69 (s, 1H), 10.95 (s, 1H), 7.71 – 7.64 (m, 2H), 7.55 – 7.41 (m, 5H), 7.39 – 7.30 (m, 2H), 7.11 – 7.04 (m, 1H), 2.54 (s, 3H).	99.6	413.0
A1003		(500MHz, DMSO) δ 12.55 (s, 1H), 7.54 – 7.34 (m, 5H), 7.27 – 7.19 (m, 2H), 7.00 – 6.91 (m, 2H), 6.86 – 6.76 (m, 1H), 3.95 – 3.80 (m, 1H), 3.75 – 3.63 (m, 1H), 3.59 – 3.43 (m, 2H), 3.30 – 3.18 (m, 2H), 3.17 – 3.08 (m, 1H), 3.02 – 2.93 (m, 1H), 2.25 (s, 3H).	99.2	482.1
A1004		(500MHz, DMSO) δ 12.54 (s, 1H), 7.58 – 7.35 (m, 5H), 3.74 – 3.54 (m, 5H), 3.51 – 3.43 (m, 1H), 3.42 – 3.34 (m, 2H), 2.25 (s, 3H).	96.5	407.0
A1005		(500MHz, DMSO) δ 11.31 (s, 1H), 8.88 (s, 1H), 8.33 (s, 1H), 8.18 (d, *J* = 8.4Hz, 1H), 7.53 – 7.47 (m, 4H), 7.47 – 7.40 (m, 2H), 2.56 (s, 3H).	100.00	414.0
A1006		(500MHz, DMSO) δ 10.51 (s, 1H), 7.52-7.40 (m, 7H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 7.3 Hz, 1H), 6.61 (t, *J* = 7.4 Hz, 1H), 5.02 (s, 2H), 2.59 (s, 3H).	96.9	428.1

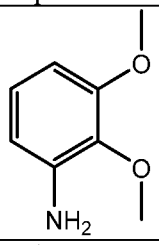
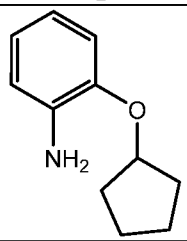
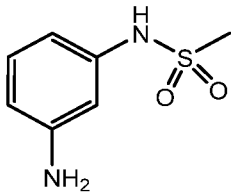
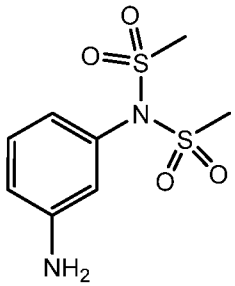
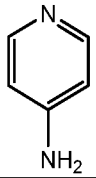
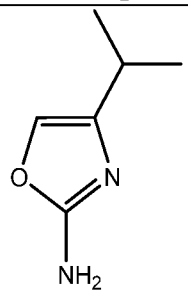
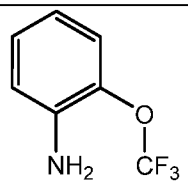
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1007		(500MHz, DMSO) δ 12.78 (s, 1H), 11.04 (s, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.6 Hz, 2H), 7.57 – 7.44 (m, 5H), 2.53 (s, 3H).	99.1	481.0
A1008		(500 MHz, DMSO) δ 12.51 (s, 1H), 8.66 (br s, 1H), 7.53 – 7.48 (m, 2H), 7.44 (d, J = 7.4 Hz, 3H), 4.22 – 4.09 (m, 1H), 2.46 (s, 3H), 1.94 – 1.81 (m, 2H), 1.72 – 1.62 (m, 2H), 1.60 – 1.51 (m, 2H), 1.51 – 1.43 (m, 2H).	100.0	405.1
A1009		(500 MHz, DMSO) δ 12.53 (s, 1H), 7.51 – 7.44 (m, 4H), 7.43 – 7.36 (m, 1H), 3.44 (t, 2H), 3.40 – 3.33 (m, 1H), 3.27 – 3.19 (m, J = 10.9, 6.3 Hz, 1H), 2.23 (s, 3H), 1.91 – 1.78 (m, 4H).	100.0	391.0
A1010		(500MHz, DMSO) δ 12.52 (s, 1H), 8.58 (s, 1H), 7.53 – 7.48 (m, 2H), 7.48 – 7.42 (m, 3H), 3.80 – 3.67 (m, 1H), 2.46 (s, 3H), 1.87 – 1.79 (m, 2H), 1.74 – 1.65 (m, 2H), 1.60 – 1.50 (m, 1H), 1.39 – 1.14 (m, 5H).	100.0	419.0
A1011		(500MHz, DMSO) δ 12.48 (s, 1H), 7.53 – 7.47 (m, 2H), 7.47 – 7.42 (m, 3H), 3.74 – 3.64 (m, 1H), 3.55 – 3.44 (m, 1H), 3.39 – 3.24 (m, 2H), 2.24 (s, 3H), 1.65 – 1.43 (m, 5H), 1.42 – 1.31 (m, 1H).	98.9	405.0
A1012		(500MHz, DMSO) δ 12.68 (s, 1H), 11.01 (s, 1H), 7.56 (d, J = 8.4Hz, 2H), 7.53 – 7.46 (m, 4H), 7.46 – 7.39 (m, 1H), 7.14 (d, J = 8.2Hz, 2H), 2.54 (s, 3H), 2.28 (s, 3H).	99.2	427.0
A1013		(500 MHz, DMSO) δ 12.56 (s, 1H), 7.55 – 7.25 (m, 10H), 4.80 – 4.43 (m, 2H), 2.88 (d, J = 7.3 Hz, 3H), 2.27 (d, J = 24.4 Hz, 3H).	100.0	441.1
A1014		(500MHz, DMSO) δ 9.40 (d, J = 8.5Hz, 1H), 8.32 (s, 1H), 7.57 (d, J = 7.4Hz, 2H), 7.45 – 7.37 (m, 2H), 7.32 – 7.22 (m, 1H), 3.88 – 3.76 (m, 1H), 2.96 – 2.82 (m, 1H), 2.03 – 1.95 (m, 1H), 1.93 – 1.86 (m, 1H), 1.72 (d, J = 4.6Hz, 2H), 1.46 – 1.21 (m, 4H)	100.0	434.1

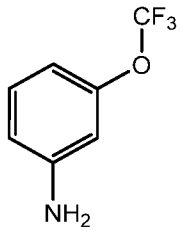
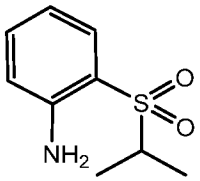
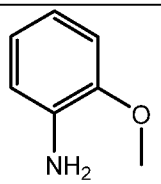
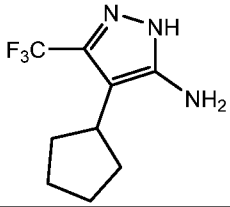
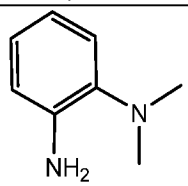
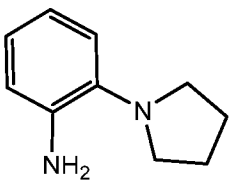
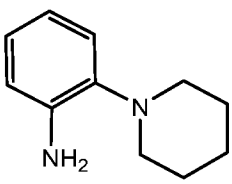
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1015		(500MHz, DMSO) δ 12.79 (s, 1H), 11.22 (s, 1H), 7.91 – 7.84 (m, 2H), 7.84 – 7.78 (m, 2H), 7.56 – 7.49 (m, 2H), 7.49 – 7.42 (m, 3H), 2.53 (s, J = 6.7Hz, 3H).	99.7	437.7
A1016		(500MHz, DMSO) δ 12.73 (s, 1H), 10.82 (s, 1H), 7.72 (d, J = 8.8Hz, 2H), 7.56 – 7.50 (m, 2H), 7.47 (dd, J = 12.7, 7.0Hz, 3H), 7.41 (d, J = 8.8Hz, 2H), 2.50 (s, 3H).	100.0	447.0
A1017		(500MHz, DMSO) δ 12.57 (s, 1H), 8.29 (d, J = 8.4Hz, 2H), 7.74 (t, J = 7.8Hz, 1H), 7.57 (d, J = 7.5Hz, 2H), 7.44 (dd, J = 10.6, 4.9Hz, 2H), 7.32 (t, J = 7.4Hz, 1H), 7.06 – 6.99 (m, 2H), 2.69 (s, 3H).	100.0	414.0
A1018		(500MHz, DMSO) δ 12.72 (s, 1H), 12.50 (s, 1H), 9.36 (s, 1H), 9.03 (s, 1H), 8.10 (s, 1H), 7.55 (d, J = 7.5Hz, 2H), 7.45 (t, J = 7.7Hz, 2H), 7.35 (t, J = 7.4Hz, 1H), 2.64 (s, 3H).	96.8	415.0
A1019		(500MHz, DMSO) δ 12.74 (s, 1H), 10.03 (s, 1H), 7.55 – 7.49 (m, 2H), 7.49 – 7.43 (m, 3H), 2.53 (s, 3H), 2.34 (s, 3H), 2.17 (s, 3H).	100.0	432.1
A1020		(500MHz, DMSO) δ 12.93 (s, 1H), 8.76 (d, J = 1.7Hz, 1H), 7.57 (d, J = 7.5Hz, 2H), 7.43 (dd, J = 10.6, 4.8Hz, 2H), 7.31 (t, J = 7.4Hz, 1H), 7.08 (d, J = 1.7Hz, 1H), 3.17 (s, 1H), 2.67 (s, 3H).	99.6	403.9
A1021		(500MHz, DMSO) δ 12.88 (s, 1H), 10.87 (s, 1H), 9.56 (s, 1H), 8.03 (d, J = 7.9 Hz, 1H), 7.54 – 7.41 (m, 6H), 7.21 (t, J = 7.7 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 2.68 (s, 3H), 2.14 (s, 3H).	99.9	470.1
A1022		(500MHz, DMSO) δ 12.88 (vbs, 1H), 11.40 (s, 1H), 9.10 (s, 1H), 8.20 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 4.4 Hz, 4H), 7.45-7.41 (m, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.31 (t, J = 7.3 Hz, 1H), 7.15 (t, J = 7.0 Hz, 1H), 3.04 (s, 3H), 2.68 (s, 3H).	95.6	506.0

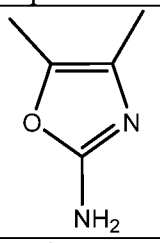
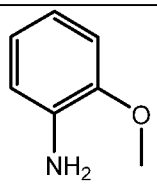
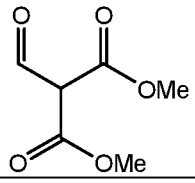
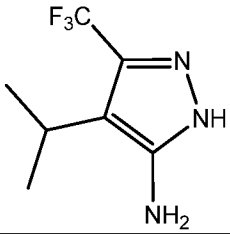
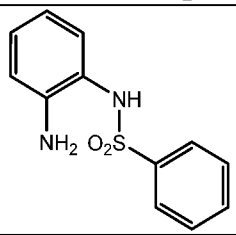
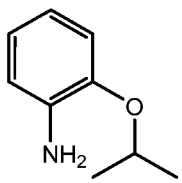
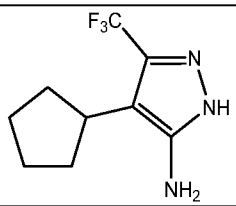
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1023		(500 MHz, DMSO) δ 12.59 (s, 1H), 9.07 (s, 1H), 7.54 – 7.42 (m, 5H), 7.41 – 7.32 (m, 4H), 7.26 (t, J = 7.2 Hz, 1H), 4.49 (d, J = 5.9 Hz, 2H), 2.48 (s, 3H).	98.2	427.1
A1024		(500MHz, DMSO) δ 9.52 (s, 1H), 8.45 – 8.38 (m, 1H), 8.37 – 8.31 (m, 1H), 7.58 – 7.35 (m, 5H), 2.68 (s, 3H).	96.9	415.0
A1025		(500MHz, DMSO) δ 12.54 (s, 1H), 8.66 (s, 1H), 7.53 – 7.48 (m, 2H), 7.48 – 7.42 (m, 3H), 4.01 – 3.90 (m, 1H), 3.85 (dt, J = 11.5, 3.7Hz, 2H), 3.42 (td, J = 11.4, 2.2Hz, 2H), 2.46 (s, 3H), 1.86 – 1.76 (m, 2H), 1.54 – 1.41 (m, 2H).	96.1	421.1
A1026		(500MHz, DMSO) δ 9.76 (s, 1H), 9.43 (s, 1H), 7.56 (d,J = 7.4Hz, 2H), 7.47 – 7.34 (m, 2H), 7.34 – 7.22 (m, 1H), 4.08 – 3.87 (m, 1H), 3.56 – 3.34 (m, 2H), 3.21 – 3.00 (m, 2H), 2.80 (s, 3H), 2.57 (s, 3H), 2.18 – 2.01 (m, 2H), 1.84 – 1.56 (m, 2H).	100.0	434.1
A1027		(500MHz, DMSO) δ 12.54 (s, 1H), 8.92 – 8.64 (m, 1H), 7.52 – 7.47 (m, 2H), 7.47 – 7.42 (m, 3H), 4.19 – 4.07 (m, 1H), 4.04 – 3.91 (m, 1H), 3.80 – 3.69 (m, 1H), 3.26 – 3.15 (m, 1H), 2.92 – 2.82 (m, 1H), 2.47 (s, 3H), 2.01 (s, 3H), 1.95 – 1.85 (m, 1H), 1.86 – 1.78 (m, 1H), 1.53 – 1.36 (m, 1H), 1.36 – 1.23 (m, 1H).	96.9	462.1
A1028		(500 MHz, DMSO) δ 13.32 (s, 1H), 7.53 (d, J = 7.6 Hz, 2H), 7.47 (m, 3H), 7.38 (t, J = 7.5 Hz, 1H), 7.19 (d, J = 5.3 Hz, 2H), 2.68 (s, 3H).	98.0	420.0
A1029		(500 MHz, DMSO) δ 12.73 (s, 1H), 11.88 (s, 1H), 7.59 – 7.50 (m, 3H), 7.47 (t, J = 7.7 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 6.59 (s, 1H), 3.76 (s, 3H), 2.64 (s, 3H).	100.0	417.1

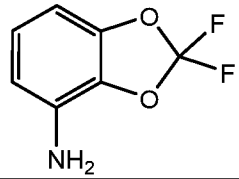
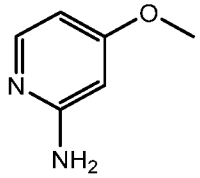
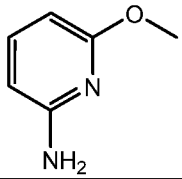
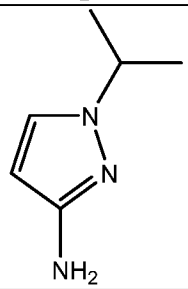
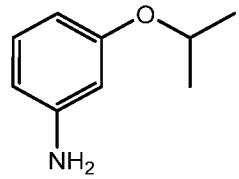
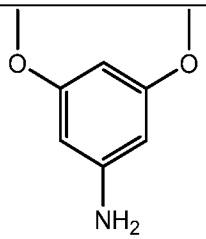
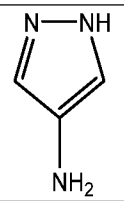
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1030		(500 MHz, DMSO) δ 12.68 (s, 1H), 10.92 (s, 1H), 7.90 (t, J = 1.9 Hz, 1H), 7.48 – 7.37 (m, 6H), 7.31 (t, J = 8.1 Hz, 1H), 7.08 (dd, J = 8.0, 1.2 Hz, 1H), 2.45 (s, 3H).	100.0	447.0
A1031		(500MHz, DMSO) δ 12.88 (s, 1H), 11.36 (s, 1H), 8.45 – 8.37 (m, 1H), 7.56 – 7.49 (m, 2H), 7.49 – 7.43 (m, 3H), 7.11 – 7.02 (m, 2H), 6.94 (ddd, J = 8.6, 6.8, 2.1Hz, 1H), 3.91 (s, 3H), 2.75 (s, 3H).	99.2	443.0
A1032		(500MHz, DMSO) δ 12.69 (s, 1H), 10.63 (s, 1H), 7.57 – 7.43 (m, 5H), 7.41 (t, J = 2.0Hz, 1H), 7.25 (t, J = 8.1Hz, 1H), 7.19 (d, J = 8.7Hz, 1H), 6.68 (dd, J = 8.1, 1.7Hz, 1H), 3.76 (s, 3H), 2.50 (s, 3H).	95.4	443.1
A1033		(500 MHz, DMSO) δ 13.00 (s, 1H), 11.74 (s, 1H), 8.44 (d, J = 7.9 Hz, 1H), 7.56 – 7.44 (m, 6H), 7.39 – 7.33 (m, 1H), 7.16 – 7.11 (m, 1H), 2.76 (s, 3H)	100.0	447.0
A1034		(500MHz, DMSO) δ 12.55 (s, 1H), 8.99 (s, 1H), 7.53 – 7.40 (m, 5H), 4.43 – 4.27 (m, 1H), 3.58 – 3.44 (m, 1H), 3.33 (d,J = 6.7Hz, 2H), 3.23 – 3.08 (m, 1H), 2.45 (s, 3H), 2.14 – 2.03 (m, 1H), 1.91 – 1.75 (m, 1H), 1.41 (s, 9H).	100.0	450.0
A1035		(400MHz, DMSO) δ 9.95 (d,J = 5.8Hz, 1H), 8.86 (s, 2H), 7.57 (d,J = 7.4Hz, 2H), 7.41 (t,J = 7.7Hz, 2H), 7.28 (t,J = 7.4Hz, 1H), 4.51 – 4.38 (m, 1H), 3.45 – 3.36 (m, 2H), 3.30 – 3.19 (m, 2H), 2.49 (s, 3H), 2.35 – 2.19 (m, 1H), 1.92 (td,J = 13.2, 6.7Hz, 1H).	99.7	406.0
A1036		(500 MHz, DMSO) δ 12.98 (br s, 1H), 11.94 (br s, 1H), 8.28 (s, 1H), 7.86 – 7.80 (m, 1H), 7.71 (t, J = 7.9 Hz, 1H), 7.54 – 7.48 (m, 4H), 7.48 – 7.42 (m, 1H), 7.29 (t, J = 7.8 Hz, 1H), 2.71 (s, 3H).	100.0	438.2

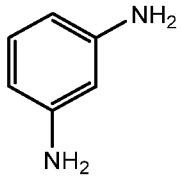
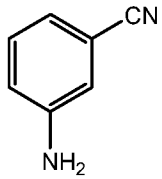
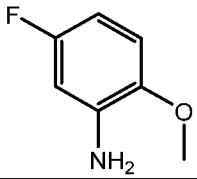
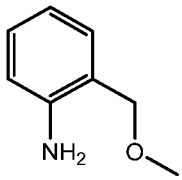
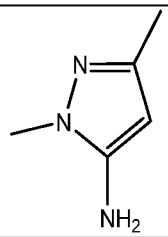
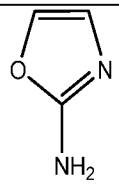
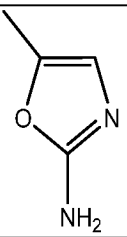
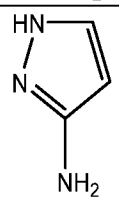
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1037		(500 MHz, DMSO) δ 12.83 (s, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.56 – 7.43 (m, 5H), 7.25 (*d*, J = 7.1 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.08 – 7.02 (m, 1H), 2.67 (s, 3H), 2.34 (s, 3H).	99.6	427.3
A1038		(400MHz, DMSO) δ 8.89 (s, 1H), 7.99 (s, 1H), 7.56 – 7.35 (m, 7H), 7.23 – 7.15 (m, 1H), 7.11 (t, J = 7.3Hz, 1H), 3.67 (s, 3H), 2.66 (s, 3H).	100.0	485.9
A1039		(400MHz, DMSO) δ 12.70 (s, 1H), 11.02 (s, 1H), 9.98 (s, 1H), 7.98 (s, 1H), 7.56 – 7.46 (m, 4H), 7.44 (s, 1H), 7.35 (d, J = 7.5Hz, 2H), 7.23 (t, J = 8.0Hz, 1H), 2.54 (d, J = 2.2Hz, 3H), 2.04 (s, 3H).	96.1	469.8
A1040		(500 MHz, DMSO) δ 13.46 (s, 1H), 7.75 (s, 1H), 7.58 – 7.44 (m, 5H), 7.40 (s, 1H), 2.68 (s, 3H).	100.0	404.1
A1041		(500 MHz, DMSO) δ 12.75 (s, 1H), 7.66 (d, J = 2.2 Hz, 1H), 7.55 – 7.43 (m, 5H), 6.58 (d, J = 2.3 Hz, 1H), 4.08 – 3.99 (m, 1H), 2.58 (s, 3H), 2.00 (d, J = 10.6 Hz, 2H), 1.81 (d, J = 13.5 Hz, 2H), 1.71 – 1.64 (m, 2H), 1.45 – 1.33 (m, 2H), 1.26 – 1.14 (m, 1H).	100.0	485.2
A1042	 Also replace **I-2** with 	(500 MHz, DMSO) δ 11.37 (s, 1H), 8.42 – 8.38 (m, 1H), 7.56 – 7.43 (m, 5H), 7.11 – 7.04 (m, 2H), 6.99 – 6.92 (m, 1H), 4.95 (s, 2H), 3.91 (s, 3H), 3.40 (s, 3H).	100.0	473.2

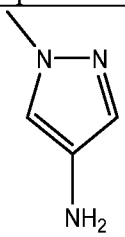
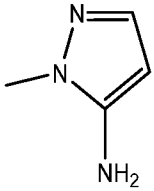
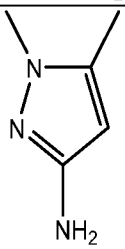
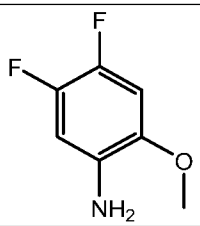
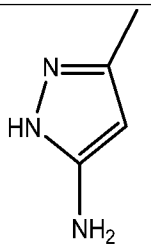
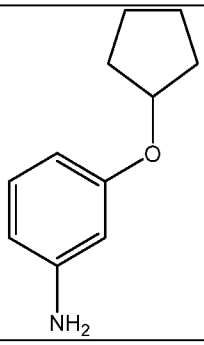
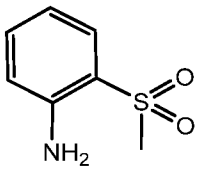
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1043		(500 MHz, DMSO) δ 12.92 (s, 1H), 11.45 (s, 1H), 8.05 (dd, J = 8.3, 1.1 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.50 – 7.45 (m, 3H), 7.05 (t, J = 8.3 Hz, 1H), 6.81 (dd, J = 8.4, 1.3 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 2.76 (s, 3H).	98.8	473.1
A1044		(500 MHz, DMSO) δ 12.91 (s, 1H), 11.40 (s, 1H), 8.43 (d, J = 8.3 Hz, 1H), 7.55 – 7.44 (m, 5H), 7.08 – 7.00 (m, 2H), 6.93 – 6.88 (m, 1H), 4.98 – 4.90 (m, 1H), 2.02 – 1.93 (m, 2H), 1.92 – 1.82 (m, 4H), 1.67 – 1.58 (m, 2H).	95.7	497.2
A1045		(500MHz, DMSO) δ 12.70 (s, 1H), 11.02 (s, 1H), 9.76 (s, 1H), 7.61 (t, J = 2.0Hz, 1H), 7.53 – 7.46 (m, 4H), 7.44 (d, J = 7.8Hz, 2H), 7.28 (t,J = 8.1Hz, 2H), 6.94 (dd, J = 8.1, 1.3Hz, 1H), 3.00 (s, 3H), 2.53 (s, 3H).	99.8	505.9
A1046		(500MHz, DMSO) δ 12.76 (s, 1H), 11.26 (s, 1H), 7.86 (s, 1H), 7.77 (d, J = 8.5Hz, 1H), 7.59 – 7.37 (m, 6H), 7.23 (d, J = 7.9Hz, 1H), 3.54 (s, 6H), 2.57 (s, 3H).	100.0	584.0
A1047		(400MHz, DMSO) δ 12.58 (s, 1H), 8.42 (s, 3H), 7.65 (s, 2H), 7.57 (d, J = 7.4Hz, 2H), 7.43 (t, J = 7.4Hz, 2H), 7.31 (t, J = 7.2Hz, 1H), 2.65 (s, 3H).	99.4	414.0
A1048		(500 MHz, DMSO) δ 13.05 (s, 1H), 8.16 (s, 1H), 7.57 (d, J = 7.3 Hz, 2H), 7.50 (d, J = 1.2 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.32 – 7.25 (m, 1H), 2.79 – 2.68 (m, 1H), 2.64 (s, 3H), 1.19 (d, J = 6.9 Hz, 6H).	99.4	446.2
A1049		(500 MHz, DMSO) δ 13.03 (s, 1H), 11.92 (s, 1H), 8.51 (d, J = 8.2 Hz, 1H), 7.55 – 7.36 (m, 7H), 7.20 (dt, J = 24.8, 9.1 Hz, 1H), 2.76 (s, 3H).	99.6	497.2

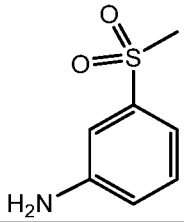
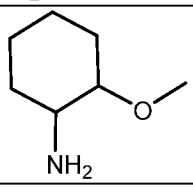
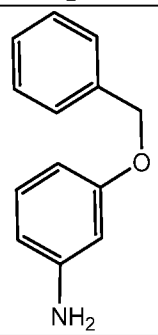
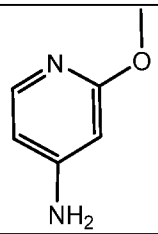
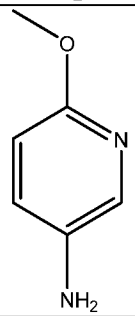
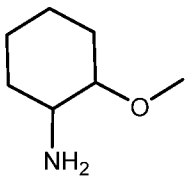
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1050		(500 MHz, DMSO) δ 12.76 (s, 1H), 11.30 (s, 1H), 7.95 (s, 1H), 7.54 – 7.41 (m, 7H), 7.08 (d, J = 8.9 Hz, 1H), 2.54 (d, J = 5.7 Hz, 3H).	99.2	497.2
A1051		(500 MHz, DMSO) δ 12.11 (s, 1H), 8.41 (d, J = 7.5 Hz, 1H), 8.22 (s, 1H), 7.84 (dd, J = 8.0, 1.6 Hz, 1H), 7.68 (t, J = 7.1 Hz, 1H), 7.58 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.30 (dd, J = 15.4, 7.9 Hz, 2H), 3.67 – 3.60 (m, 1H), 2.63 (s, 3H), 1.21 – 1.18 (m, 6H).	98.6	519.2
A1052	 Also replace **I-1** with 	(500 MHz, DMSO) δ 12.48 (s, 1H), 11.30 (s, 1H), 8.40 (d, J = 8.0 Hz, 1H), 7.11 – 7.02 (m, 2H), 6.98 – 6.90 (m, 1H), 3.89 (s, 3H), 3.41 – 3.28 (m, 1H), 2.81 (s, 3H), 2.01 – 1.89 (m, 2H), 1.87 – 1.60 (m, 6H).	97.1	435.2
A1053		(500 MHz, DMSO) δ 12.86 (s, 1H), 11.33 (s, 1H), 8.43 – 8.34 (m, 1H), 7.56 – 7.43 (m, 5H), 7.26 – 7.19 (m, 1H), 7.12 – 6.99 (m, 2H), 2.75 (s, 3H), 2.68 (s, 6H).	99.7	456.2
A1054		(500 MHz, DMSO) δ 8.08 (d, *J* = 8.2 Hz, 1H), 7.50 (d, *J* = 4.5 Hz, 4H), 7.46 – 7.38 (m, 1H), 7.08 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.06 – 6.99 (m, 1H), 6.97 – 6.91 (m, 1H), 3.13 – 3.07 (m, 4H), 2.71 (s, 3H), 1.97 – 1.87 (m, 4H).	99.7	482.3
A1055		(500 MHz, DMSO) δ 11.60 (s, 1H), 8.43 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.54 – 7.46 (m, 4H), 7.45 – 7.38 (m, 1H), 7.18 (dd, J = 7.6, 1.7 Hz, 1H), 7.10 – 6.98 (m, 2H), 2.83 – 2.77 (m, 4H), 2.74 (s, 3H), 1.84 – 1.76 (m, 4H), 1.61 – 1.51 (m, 2H).	100	496.3

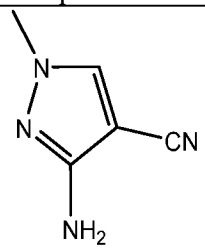
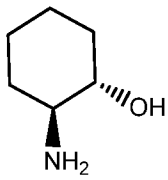
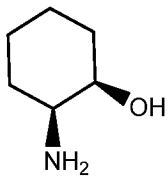
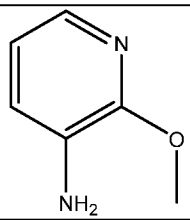
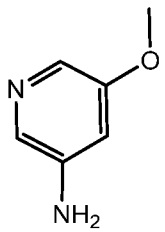
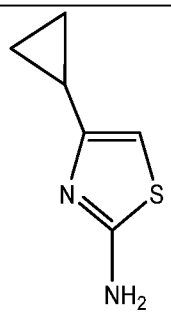
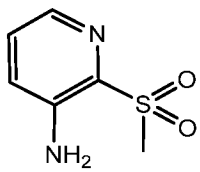
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1056		(500 MHz, DMSO) δ 12.91 (s, 1H), 8.30 (s, 1H), 7.57 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.31 (t, J = 7.4 Hz, 1H), 2.63 (s, 3H), 2.21 (s, 3H), 1.99 (s, 3H).	95.6	432.3
A1057	 Also replace **I-2** with 	(500 MHz, MeOD) δ 8.77 (s, 1H), 8.42 (dd, J = 8.0, 1.5 Hz, 1H), 7.59 – 7.43 (m, 5H), 7.15 – 7.04 (m, 2H), 7.02 – 6.90 (m, 1H), 4.01 (s, 3H).	99.9	429.8
A1058		(500 MHz, DMSO) δ 13.45 (s, 2H), 7.56 – 7.43 (m, 14H), 3.08 – 2.99 (m, 3H), 2.69 (s, 8H), 1.28 (d, *J* = 7.1 Hz, 6H).	99.5	513.3
A1059		(500MHz, DMSO) δ 8.37 – 8.17 (m, 1H), 8.02 – 7.90 (m, 1H), 7.68 (d, J = 7.4Hz, 2H), 7.61 (d, J = 7.8Hz, 2H), 7.55 – 7.47 (m, 1H), 7.47 – 7.36 (m, 5H), 7.35 – 7.27 (m, 1H), 7.12 – 7.01 (m, 1H), 6.97 – 6.82 (m, 2H), 2.65 (s, 2H).	96.1	568.0
A1060		(500 MHz, DMSO) δ 12.89 (s, 1H), 11.41 (s, 1H), 8.42 (dd, J = 8.1, 1.5 Hz, 1H), 7.56 – 7.40 (m, 5H), 7.13 – 7.08 (m, 1H), 7.03 (td, J = 7.8, 1.6 Hz, 1H), 6.96 – 6.88 (m, 1H), 4.75 – 4.64 (m, 1H), 2.78 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H).	99.2	471.2
A1061		(500 MHz, DMSO) δ 13.48 (s, 1H), 7.54 – 7.43 (m, 5H), 3.06 – 2.94 (m, 1H), 2.68 (s, 3H), 1.93 – 1.56 (m, 8H).	98.1	539.3

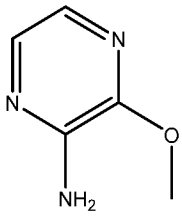
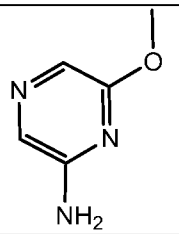
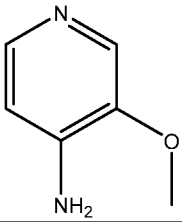
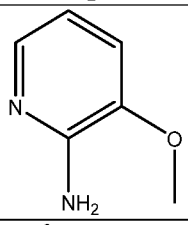
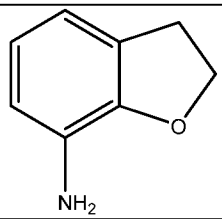
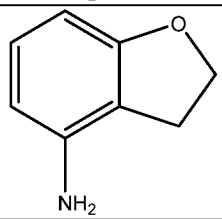
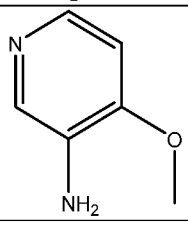
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1062		(500 MHz, DMSO) δ 12.89 (s, 1H), 11.42 (s, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.60 – 7.42 (m, 5H), 7.25 – 7.13 (m, 2H), 2.65 (s, 3H).	99.8	493.2
A1063		(500 MHz, DMSO) δ 12.54 (s, 1H), 8.17 – 8.07 (m, 2H), 7.93 (d, J = 1.9 Hz, 1H), 7.57 (d, J = 7.4 Hz, 2H), 7.45 (dd, J = 10.6, 4.9 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 6.67 (dd, J = 5.8, 2.4 Hz, 1H), 3.86 (s, 3H), 2.69 (s, 3H).	98.6	444.9
A1064		(500 MHz, DMSO) δ 13.00 – 12.58 (m, 1H), 11.89 – 11.30 (m, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.70 (t, J = 7.9 Hz, 1H), 7.54 – 7.37 (m, 5H), 6.53 (d, J = 8.0 Hz, 1H), 3.85 (s, 3H), 2.65 (s, 3H).	99.5	444.9
A1065		(500 MHz, DMSO) δ 12.64 (s, 1H), 11.22 (s, 1H), 7.59 (d, J = 2.2 Hz, 1H), 7.48 – 7.35 (m, 5H), 6.51 (d, J = 2.3 Hz, 1H), 4.39 – 4.29 (m, 1H), 2.51 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H).	99.3	445.2
A1066		(500 MHz, DMSO) δ 12.70 (s, 1H), 10.61 (s, 1H), 7.56 – 7.51 (m, 2H), 7.50 – 7.44 (m, 3H), 7.40 (t, J = 2.1 Hz, 1H), 7.23 (t, J = 8.1 Hz, 1H), 7.16 – 7.13 (m, 1H), 6.66 (dd, J = 8.2, 1.8 Hz, 1H), 4.63 – 4.53 (m, 1H), 1.29 (s, 3H), 1.28 (s, 3H).	99.5	471.2
A1067		(500 MHz, DMSO) δ 12.69 (s, 1H), 7.54 – 7.41 (m, 5H), 6.93 (d, *J* = 2.2 Hz, 2H), 6.25 (dd, *J* = 2.5, 2.2 Hz, 1H), 3.74 (s, 6H), 2.52 (s, 3H).	95.5	473.8
A1068		(500 MHz, DMSO) δ 12.66 (s, 1H), 10.89 (s, 1H), 7.83 (s, 3H), 7.55 – 7.39 (m, 5H), 2.56 (s, 3H).	99.4	403.2

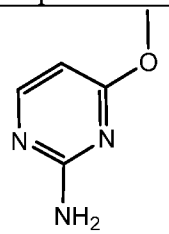
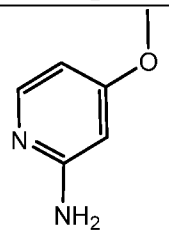
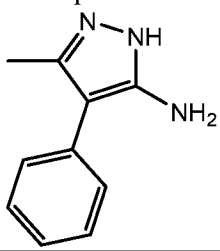
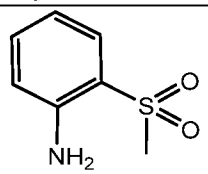
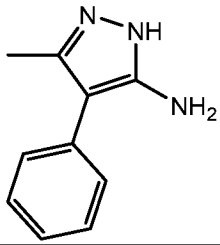
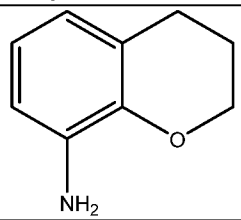
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1069		(400MHz, DMSO) δ 11.98 (s, 1H), 8.13 (s, 1H), 7.58 (d, J = 7.6Hz, 2H), 7.42 (t, J = 7.5Hz, 2H), 7.29 (t, J = 7.3Hz, 1H), 7.06 (s, 1H), 6.92 (t, J = 7.8Hz, 1H), 6.72 (d, J = 7.6Hz, 1H), 6.22 (d, J = 8.0Hz, 1H), 2.65 (s, 3H).	98.4	428.0
A1070		(500 MHz, DMSO) δ 12.78 (s, 1H), 8.27 (s, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.59 – 7.47 (m, 6H), 7.46 – 7.40 (m, 1H), 2.57 (s, 3H).	98.4	438.1
A1071		(500 MHz, DMSO) δ 12.97 (s, 1H), 11.59 (s, 1H), 8.30 (dd, J = 11.3, 3.2 Hz, 1H), 7.56 – 7.45 (m, 5H), 7.09 (dd, J = 9.1, 5.2 Hz, 1H), 6.91 – 6.85 (m, 1H), 3.92 (s, 3H), 2.78 (s, 3H).	100.0	461.1
A1072		(500 MHz, DMSO) δ 12.86 (s, 1H), 10.85 (s, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.56 – 7.45 (m, 5H), 7.39 (dd, J = 7.6, 1.3 Hz, 1H), 7.37 – 7.32 (m, 1H), 7.14 (td, J = 7.5, 1.0 Hz, 1H), 4.52 (s, 2H), 3.38 (s, 3H), 2.70 (s, 3H).	100.0	425.1
A1073		(500 MHz, DMSO) δ 12.82 (s, 1H), 11.34 (s, 1H), 7.55 – 7.38 (m, 5H), 6.19 (s, 1H), 3.68 (s, 3H), 2.62 (s, 3H), 2.12 (s, 3H).	99.8	431.9
A1074		(500 MHz, DMSO) δ 13.10 (s, 1H), 7.84 (s, 1H), 7.55 (d, J = 14.4 Hz, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.07 (s, 1H), 2.65 (s, 3H).	98.4	404.1
A1075		(500 MHz, DMSO) δ 12.96 (s, 1H), 8.21 (s, 1H), 7.57 (d, J = 7.3 Hz, 2H), 7.46 – 7.41 (m, 2H), 7.34 – 7.29 (m, 1H), 6.68 (d, J = 1.3 Hz, 1H), 2.63 (s, 3H), 2.28 (s, 3H).	96.4	418.1
A1076		(500 MHz, DMSO) δ 12.73 (s, 1H), 12.36 (s, 1H), 7.61 (s, 1H), 7.56 – 7.46 (m, 4H), 7.40 (t, J = 7.9 Hz, 1H), 6.62 (s, 1H), 2.63 (s, 3H).	100.0	403.2

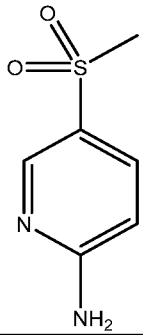
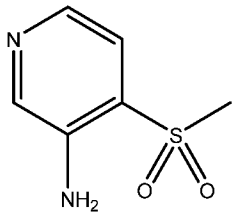
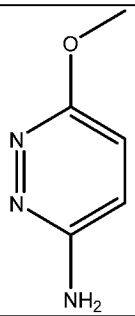
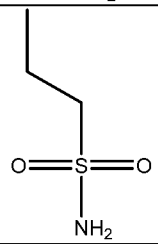
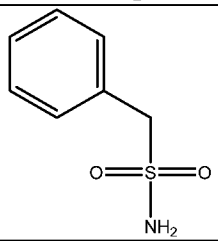
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1077		(500 MHz, DMSO) δ 7.94 (s, 1H), 7.47 (d, J = 7.5 Hz, 2H), 7.43 (d, J = 0.6 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.31 – 7.25 (m, 1H), 3.74 (s, 3H), 2.53 (s, 3H).		417.1
A1078		(500 MHz, DMSO) δ 12.74 (s, 1H), 11.90 (br s, 1H), 7.54 – 7.46 (m, 4H), 7.44 – 7.38 (m, 1H), 7.34 (d, J = 1.8 Hz, 1H), 6.39 (d, J = 1.8 Hz, 1H), 3.77 (s, 3H), 2.65 (s, 3H).		417.1
A1079		(500 MHz, DMSO) δ 12.73 (s, 1H), 11.64 (br s, 1H), 7.54 – 7.45 (m, 4H), 7.42 – 7.36 (m, 1H), 6.43 (s, 1H), 3.64 (s, 3H), 2.62 (s, 3H), 2.24 (s, 3H).		431.2
A1080		(500 MHz, DMSO) δ 12.86 (s, 1H), 11.12 (s, 1H), 8.06 (dd, J = 13.1, 7.4 Hz, 1H), 7.49 – 7.36 (m, 5H), 7.24 (dd, J = 12.4, 7.9 Hz, 1H), 3.78 (s, 3H), 2.62 (s, 3H).		479.2
A1081		(500 MHz, DMSO) δ 12.24 (s, 1H), 11.85 (s, 1H), 7.58 (d, J = 7.4 Hz, 2H), 7.47 – 7.39 (m, 2H), 7.33 – 7.26 (m, 1H), 6.41 (s, 1H), 5.90 (br s, 1H), 2.67 (s, 3H), 2.21 (s, 3H).		417.1
A1082		(500 MHz, DMSO) δ 12.69 (s, 1H), 10.67 (s, 1H), 7.55 – 7.50 (m, 2H), 7.47 (t, J = 6.8 Hz, 3H), 7.39 (t, J = 2.1 Hz, 1H), 7.22 (t, J = 8.1 Hz, 1H), 7.13 (d, J = 9.0 Hz, 1H), 6.63 (dd, J = 8.2, 1.8 Hz, 1H), 4.84 – 4.73 (m, 1H), 1.97 – 1.86 (m, 2H), 1.77 – 1.66 (m, 4H), 1.65 – 1.54 (m, 2H).		497.2
A1083		(500 MHz, DMSO) δ 12.97 (s, 1H), 11.13 (s, 1H), 8.40 (d, J = 8.2 Hz, 1H), 7.94 (dd, J = 8.0, 1.5 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 7.55 – 7.45 (m, 5H), 7.40 (t, J = 7.7 Hz, 1H), 3.35 (s, 3H), 2.69 (s, 3H).	96.6	491.2

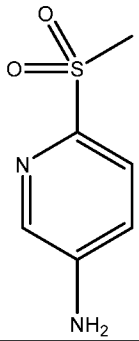
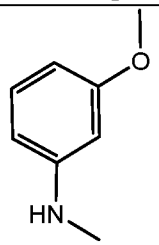
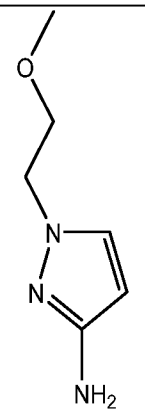
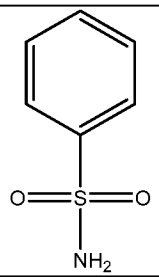
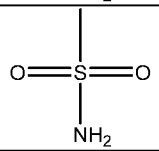
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1084		(500 MHz, DMSO) δ 12.76 (s, 1H), 11.10 (s, 1H), 8.41 (s, 1H), 7.90 (s, 1H), 7.64 (d, J = 5.0 Hz, 2H), 7.55 – 7.42 (m, 5H), 3.23 (s, 3H), 2.54 (s, 3H).	99.7	491.2
A1085		(500 MHz, DMSO) δ 12.58 (s, 1H), 8.82 (s, 1H), 7.58 – 7.34 (m, 5H), 4.07 – 3.95 (m, 1H), 3.42 – 3.37 (m, 1H), 3.29 (s, 3H), 2.56 (s, 3H), 1.91 – 1.83 (m, 1H), 1.66 – 1.27 (m, 7H).	98.9	449.2
A1086		(500 MHz, MeOD) δ 7.53 – 7.44 (m, 8H), 7.37 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.4 Hz, 1H), 7.25 (t, J = 8.1 Hz, 1H), 7.17 (d, J = 8.8 Hz, 1H), 6.78 (dd, J = 8.2, 2.4 Hz, 1H), 5.11 (s, 2H), 2.70 (s, 3H).		519.2
A1087		(500 MHz, DMSO) δ 11.06 (s, 1H), 8.06 (d, J = 5.0 Hz, 1H), 7.54-7.42 (m, 6H), 7.23 (s, 1H), 7.13 (d, J = 5.7 Hz, 1H), 3.84 (s, 3H), 2.50 (s, 3H).	100	444.2
A1088		(500 MHz, DMSO) δ 12.72 (s, 1H), 10.97 (s, 1H), 8.45 (d, J = 2.6 Hz, 1H), 8.02 (dd, J = 8.9, 2.7 Hz, 1H), 7.54 – 7.41 (m, 5H), 6.84 (d, J = 8.8 Hz, 1H), 3.84 (s, 3H), 2.54 (s, 3H).	100	444.1
A1089		(500 MHz, DMSO-d6) δ 12.53 (s, 1H), 7.47 (s, 4H), 7.41 (s, 1H), 3.86 – 3.73 (m, 1H), 3.29 (s, 3H), 3.17 – 3.06 (m, 1H), 2.52 (s, 3H), 2.03 – 1.86 (m, 2H), 1.70 – 1.55 (m, 2H), 1.37 – 1.20 (m, 4H).	95.8	449.2

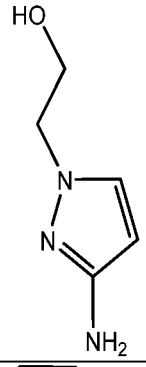
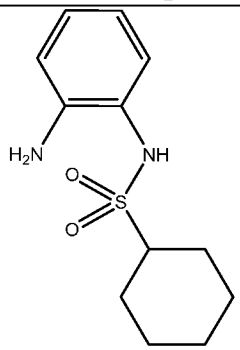
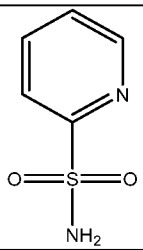
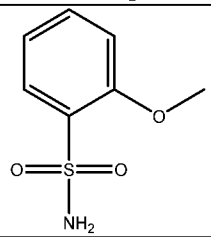
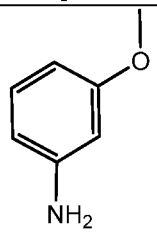
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1090		(500 MHz, DMSO) δ 12.38 (s, 1H), 8.31 (s, 1H), 8.20 (s, 1H), 7.51 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.7 Hz, 2H), 7.24 (t, J = 7.4 Hz, 1H), 3.75 (s, 3H), 2.58 (s, 3H).		442.2
A1091		(500 MHz, DMSO) δ 12.53 (s, 1H), 7.55 – 7.39 (m, 5H), 4.65 (s, 1H), 3.68 – 3.52 (m, 1H), 3.37 – 3.31 (m, 1H), 2.51 (s, 3H), 1.98 – 1.91 (m, 1H), 1.89 – 1.82 (m, 1H), 1.68 – 1.56 (m, 2H), 1.33 – 1.15 (m, 4H).	97.1	435.2
A1092		(500 MHz, DMSO) δ 12.57 (s, 1H), 8.73 (s, 1H), 7.59 – 7.36 (m, 5H), 4.65 (s, 1H), 3.89 – 3.82 (m, 1H), 3.80 – 3.76 (m, 1H), 2.57 (s, 3H), 1.72 – 1.45 (m, 6H), 1.37 – 1.25 (m, 2H).	97.8	435.3
A1093		(500 MHz, DMSO) δ 12.97 (s, 1H), 11.46 (s, 1H), 8.66 (dd, J = 7.8, 1.7 Hz, 1H), 7.87 (dd, J = 5.0, 1.7 Hz, 1H), 7.58 – 7.41 (m, 5H), 7.01-6.98 (m, 1H), 4.00 (s, 3H), 2.76 (s, 3H).	99.0	444.1
A1094		(500 MHz, CD_3CN) δ 12.48 (s, 1H), 8.28 (d, *J* = 1.7 Hz, 1H), 7.97 (s, 1H), 7.94 – 7.92 (m, 1H), 7.88 (d, *J* = 2.5 Hz, 1H), 7.54 (d, *J* = 7.4 Hz, 2H), 7.39 – 7.35 (m, 2H), 7.30 – 7.25 (m, 1H), 3.80 (s, 3H), 2.67 (s, 3H).	99.0	444.1
A1095		(500 MHz, DMSO) δ 13.40 (s, 1H), 12.73 (s, 1H), 7.56 (s, 1H), 7.55 (s, 1H), 7.48 – 7.43 (m, 2H), 7.35 (t, J = 7.3 Hz, 1H), 6.71 (s, 1H), 2.68 (s, 3H), 2.02 – 1.95 (m, 1H), 0.88 – 0.76 (m, 4H).	98.0	460.2
A1096		(500 MHz, DMSO) δ 12.14 (s, 1H), 8.85 (dd, *J* = 8.5, 1.2 Hz, 1H), 8.39 (d, *J* = 3.3 Hz, 1H), 7.74 – 7.66 (m, 1H), 7.56 (s, 1H), 7.54 (s, 1H), 7.50 – 7.42 (m, 2H), 7.36 (t, *J* = 7.3 Hz, 1H), 3.40 (s, 3H), 2.70 – 2.60 (m, 3H).	96.0	491.2

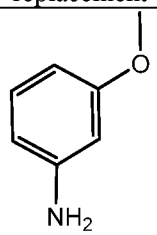
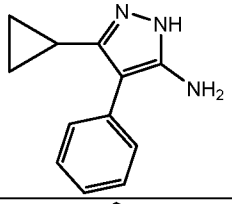
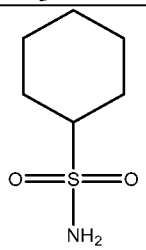
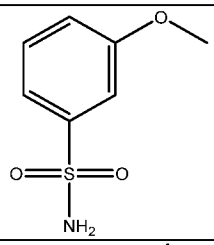
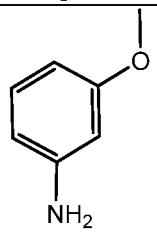
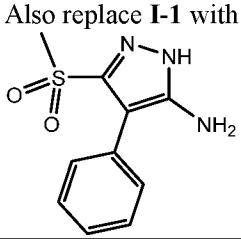
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1097		(500MHz, CD_3CN) δ 8.05 (s, 1H), 7.83 (d,J = 2.9Hz, 1H), 7.73 (d,J = 3.0Hz, 1H), 7.61 (d,J = 7.2Hz, 1H), 7.46 – 7.41 (m, 2H), 7.30 (dd,J = 3.8, 2.7Hz, 1H), 7.22 (dd,J = 2.7, 1.6Hz, 1H), 7.01 (dd,J = 4.1, 1.6Hz, 1H), 4.01 (s, 3H), 2.89 (s, 3H).	95.6	445.2
A1098		(500 MHz, DMSO) δ 12.83 (s, 1H), 9.10 (s, 1H), 8.13 (s, 1H), 7.93 (s, 1H), 7.58 (s, 1H), 7.56 (s, 1H), 7.46 – 7.40 (m, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 3.91 (s, 3H), 2.69 (s, 3H).	99.8	445.2
A1099		(500 MHz, DMSO) δ 13.10 (s, 1H), 8.64 (s, 1H), 8.34 (s, 1H), 8.22 (s, 1H), 8.13 (s, 1H), 7.57 (s, 1H), 7.56 (s, 1H), 7.46 – 7.41 (m, 2H), 7.34 – 7.29 (m, 1H), 4.04 (s, 3H), 2.69 (s, 3H).	99.2	444.3
A1100		(500 MHz, DMSO) δ 12.74 (s, 1H), 8.14 (s, 1H), 7.93 (d, *J* = 5.2 Hz, 1H), 7.59 (s, 1H), 7.58 (s, 1H), 7.48 – 7.42 (m, 2H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.18 (s, 1H), 3.95 (s, 3H), 2.69 (s, 3H).	99.6	444.1
A1101		(500 MHz, DMSO) δ 12.86 (s, 1H), 11.15 (s, 1H), 8.07 (t, *J* = 6.3 Hz, 1H), 7.51 – 7.44 (m, 5H), 6.96 (dd, *J* = 7.3, 0.8 Hz, 1H), 6.80 (t, *J* = 7.7 Hz, 1H), 4.64 – 4.60 (m, 2H), 3.27 – 3.22 (m, 2H), 2.70 (s, 3H).	100	455.3
A1102		(500 MHz, DMSO) δ 12.75 (s, 1H), 8.13 (s, 1H), 7.69 (s, 1H), 7.56 – 7.43 (m, 4H), 7.38 (s, 1H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.49 (d, *J* = 7.8 Hz, 1H), 4.62 – 4.55 (m, 2H), 3.23 – 3.17 (m, 2H), 2.66 (s, 3H).	100	455.2
A1103		(500 MHz, DMSO) δ 12.87 (s, 1H), 9.67 (s, 1H), 8.40 (d, *J* = 5.4 Hz, 1H), 7.58 (s, 1H), 7.56 (s, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.45 (m, 3H), 7.33 (t, *J* = 7.4 Hz, 1H), 4.15 (s, 3H), 2.71 (s, 3H).	97.9	444.2

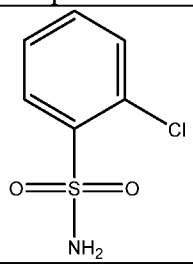
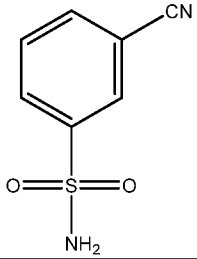
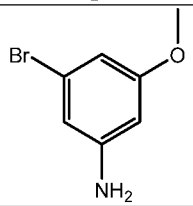
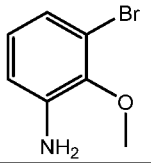
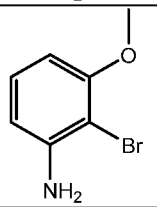
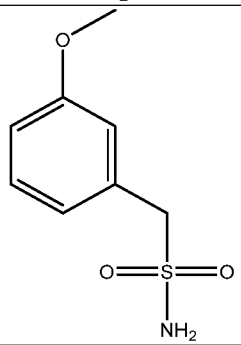
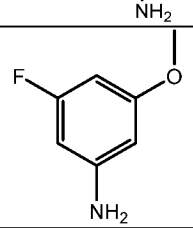
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1104		(500 MHz, DMSO) δ 12.79 (s, 1H), 8.31 (d, *J* = 5.6 Hz, 1H), 8.19 (s, 1H), 7.61 – 7.51 (m, 2H), 7.46 – 7.35 (m, 2H), 7.32 – 7.23 (m, 1H), 6.52 (d, *J* = 5.6 Hz, 1H), 3.92 (s, 3H), 2.63 (s, 3H).	93.0	445.2
A1105	 Also replace **I-1** with 	(500 MHz, DMSO) δ 12.54 – 12.46 (m, 1H), 11.82 – 11.67 (m, 1H), 8.14 (t, J = 5.9 Hz, 1H), 7.86 (s, 1H), 7.53-7.46 (m, 4H), 7.41-7.36 (m, 1H), 6.74-6.71 (m, 1H), 3.85 (s, 3H), 2.71 (s, 3H), 2.33 (s, 3H)	97.9	390.3
A1106	 Also replace **I-1** with 	(500 MHz, DMSO) δ 12.56 (s, 1H), 11.49 – 11.15 (m, 1H), 8.40 (d, J = 8.4 Hz, 1H), 7.92 (dd, J = 7.9, 1.5 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 7.55-7.48 (m, 4H), 7.36 (t, J = 7.5 Hz, 2H), 3.33 (s, 3H), 2.70 (s, 3H), 2.34 (s, 3H).	100	437.25
A1107		(500 MHz, DMSO) δ 11.91 (s, 1H), 8.26 (d, *J* = 6.6 Hz, 1H), 8.12 (s, 1H), 7.55 – 7.32 (m, 5H), 6.77 – 6.68 (m, 2H), 4.29 – 4.25 (m, 2H), 2.77 – 2.73 (m, 2H), 2.69 (s, 3H), 1.99 – 1.93 (m, 2H).	99.3	469.3

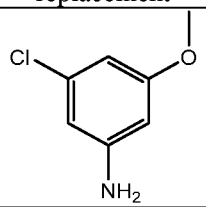
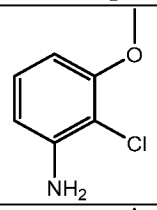
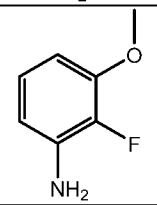
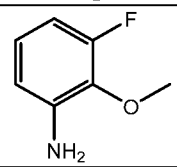
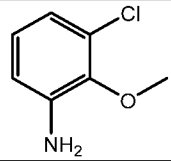
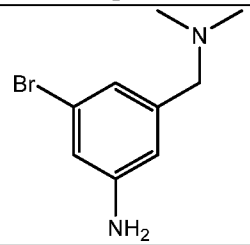
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1108		(500 MHz, CD_3CN) δ 13.03 (s, 1H), 8.64 (d, *J* = 2.4 Hz, 1H), 8.44 (d, *J* = 8.9 Hz, 1H), 8.02 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.92 (s, 1H), 7.48 (s, 1H), 7.46 (s, 1H), 7.33 – 7.29 (m, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 2.96 (s, 3H), 2.61 (s, 3H).	92.4	491.2
A1109		(500 MHz, CD_3CN) δ 12.10 (s, 1H), 9.51 (s, 1H), 8.28 (d, *J* = 5.0 Hz, 1H), 7.86 (d, *J* = 17.0 Hz, 1H), 7.59 (d, *J* = 5.0 Hz, 1H), 7.36 (s, 1H), 7.35 (s, 1H), 7.25 – 7.19 (m, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 3.06 (s, 3H), 2.50 (s, 3H).	96.7	492.2
A1110		(500 MHz, CD_3CN) δ 12.53 (s, 1H), 8.32 (s, 1H), 7.85 (s, 1H), 7.38 (s, 1H), 7.36 (s, 1H), 7.26 – 7.22 (m, 2H), 7.17 – 7.13 (m, 1H), 6.87 (d, *J* = 9.3 Hz, 1H), 3.83 (s, 3H), 2.55 (s, 3H).	99.8	445.2
A1111		(500 MHz, DMSO) δ 12.45 (s, 1H), 7.55 – 7.40 (m, 5H), 3.47 (dt, J = 15.5, 7.0 Hz, 2H), 2.57 (s, 3H), 1.76 (dt, J = 15.0, 7.5 Hz, 2H), 1.02 (t, J = 7.5 Hz, 3H).	96.2	443.1
A1112		(500 MHz, CDCl3) δ 12.41 (s, 1H), 7.53 – 7.41 (m, 5H), 7.40-7.36 (m, 5H), 4.83 (s, 2H), 2.65 – 2.60 (m, 3H).	100	489.2 (M-H)

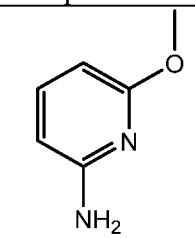
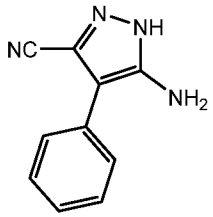
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1113		(500 MHz, DMSO) δ 12.48 (s, 1H), 8.93 (d, *J* = 1.9 Hz, 1H), 8.50 (dd, *J* = 8.6, 2.1 Hz, 1H), 8.12 (s, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.56 – 7.32 (m, 5H), 3.23 (s, 3H), 2.63 (s, 3H).	99.6	492.0
A1114		(500 MHz, DMSO) δ 12.70 (s, 1H), 8.13 (s, 1H), 7.49 (s, 1H), 7.47 (s, 1H), 7.42 – 7.34 (m, 2H), 7.27 (s, 1H), 7.14 (s, 1H), 6.93 (s, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.71 (s, 1H), 3.65 (s, 3H), 3.31 (s, 3H), 2.13 (s, 3H).	100.0	457.3
A1115		(500 MHz, DMSO) δ 12.73 (s, 1H), 11.27 (s, 1H), 7.58 (d, *J* = 2.2 Hz, 1H), 7.51 – 7.40 (m, 5H), 6.56 (d, *J* = 2.2 Hz, 1H), 4.18 – 4.11 (m, 2H), 3.66 – 3.61 (m, 2H), 3.20 (s, 3H), 2.56 (s, 3H).	99.6	461.1
A1116		(500 MHz, DMSO) δ 13.31 (s, 1H), 8.09 – 8.04 (m, 2H), 7.77 (t, J = 7.4 Hz, 1H), 7.70 (t, J = 7.6 Hz, 2H), 7.53 (dt, J = 15.2, 7.5 Hz, 4H), 7.44 (d, J = 7.2 Hz, 1H), 2.50 (s, 3H).	98.5	477.1
A1117		(500 MHz, DMSO) δ 8.34 (s, 1H), 7.55 (d, J = 7.7 Hz, 2H), 7.44 (dd, J = 10.6, 4.9 Hz, 2H), 7.33 (dd, J = 10.5, 4.3 Hz, 1H), 3.33 (s, 3H), 2.62 (s, 3H).	97.0	413.1 (M-H)

Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1118		(500 MHz, DMSO) δ 12.04 (s, 1H), 8.13 (s, 1H), 7.57 – 7.29 (m, 6H), 6.57 (s, 1H), 4.86 (s, 1H), 4.03 (s, 2H), 3.71 (s, 2H), 2.64 (s, 3H).	99.3	447.4
A1119		(500 MHz, DMSO) δ 12.25 (s, 1H), 8.26 (s, 1H), 7.77 (dd, J = 8.1, 1.4 Hz, 1H), 7.52 (d, J = 7.4 Hz, 2H), 7.41 – 7.33 (m, 2H), 7.30 (dd, J = 8.0, 1.5 Hz, 1H), 7.26 – 7.20 (m, 1H), 7.18 – 7.12 (m, 1H), 7.06 – 7.00 (m, 1H), 2.97 – 2.94 (m, 1H), 2.58 (s, 3H), 1.95 (d, J = 10.9 Hz, 2H), 1.56 (d, J = 13.1 Hz, 2H), 1.43 (d, J = 12.4 Hz, 1H), 1.31 – 1.19 (m, 2H), 1.13 – 1.03 (m, 2H), 1.02 – 0.93 (m, 1H).	96.4	574.1
A1120		(500 MHz, DMSO) δ 8.72 (dt, J = 4.7, 1.3 Hz, 1H), 8.15 – 8.13 (m, 2H), 7.70 (dd, J = 8.8, 4.6 Hz, 1H), 7.53 (d, J = 7.4 Hz, 2H), 7.43 (dd, J = 10.6, 4.9 Hz, 2H), 7.32 (t, J = 7.4 Hz, 1H), 2.43 (s, 3H).	96.7	478.2
A1121		(500 MHz, DMSO) δ 7.91 (dd, J = 7.9, 1.7 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.49 – 7.45 (m, 4H), 7.42 (s, 1H), 7.24 (d, J = 8.2 Hz, 1H), 7.19 – 7.13 (m, 1H), 3.86 (s, 3H), 2.45 (s, 3H).	96.9	507.3
A1122	 Also replace **I-1** with 	(500 MHz, DMSO) δ 12.34 (brs, 1H), 7.60-7.54 (m, 2H), 7.49 (t, J = 7.7 Hz, 2H), 7.42 (t, J = 2.1 Hz, 1H), 7.36 (t, J = 7.2 Hz, 1H), 7.27-7.22 (m, 1H), 7.21-7.17 (m, 1H), 3.77 (s, 3H), 2.58(s, 3H), 2.58 (overlapping s, 3H).	97.6	421.1

Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1123	 Also replace **I-1** with 	(500 MHz, DMSO) δ 7.67-7.62 (m, 2H), 7.49 (t, J = 7.7 Hz, 2H), 7.42 (m, 1H), 7.37-7.32 (m, 1H), 7.25-7.20 (m, 1H), 7.15 (m, 1H), 6.63 (dd, J = 8.1, 1.0 Hz, 1H), 3.76 (s, 3H), 2.59 (s, 3H), 1.98-1.90 (m, 1H), 1.02-0.95 (m, 4H).	98.2	415.2
A1124		(500 MHz, DMSO) δ 13.08 (s, 1H), 7.54 (d, J = 7.3 Hz, 2H), 7.46 – 7.41 (m, 2H), 7.34 – 7.30 (m, 1H), 3.51 (tt, J = 12.2, 3.5 Hz, 2H), 2.59 (s, 3H), 2.04 (d, J = 10.7 Hz, 2H), 1.82 (d, J = 13.2 Hz, 2H), 1.63 (d, J = 12.4 Hz, 1H), 1.48 (qd, J = 12.5, 3.3 Hz, 2H), 1.33 – 1.23 (m, 2H), 1.16 (dd, J = 25.3, 12.6 Hz, 1H).	100	483.3
A1125		(500 MHz, DMSO) δ 13.78 – 13.56 (m, 1H), 8.15 (s, 1H), 7.57 – 7.50 (m, 4H), 7.47 (dd, J = 2.5, 1.2 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.33 – 7.28 (m, 1H), 7.27 – 7.24 (m, 1H), 3.83 (s, 3H), 2.48 (s, 3H).	97.1	507.3
A1126	 Also replace **I-1** with 	(500 MHz, DMSO) δ 12.72 (brs, 1H), 7.70 (brs, 2H), 7.43-7.47 (m, 3H), 7.35-7.41 (m, 1H), 7.22-7.25 (m, 1H), 7.16-7.18 (m, 1H), 6.62-6.67 (m, 1H), 3.77 (s, 3H), 3.35 (s, 3H), 2.60 (s, 3H), 2.55 (s, 3H).	99.3	453.5

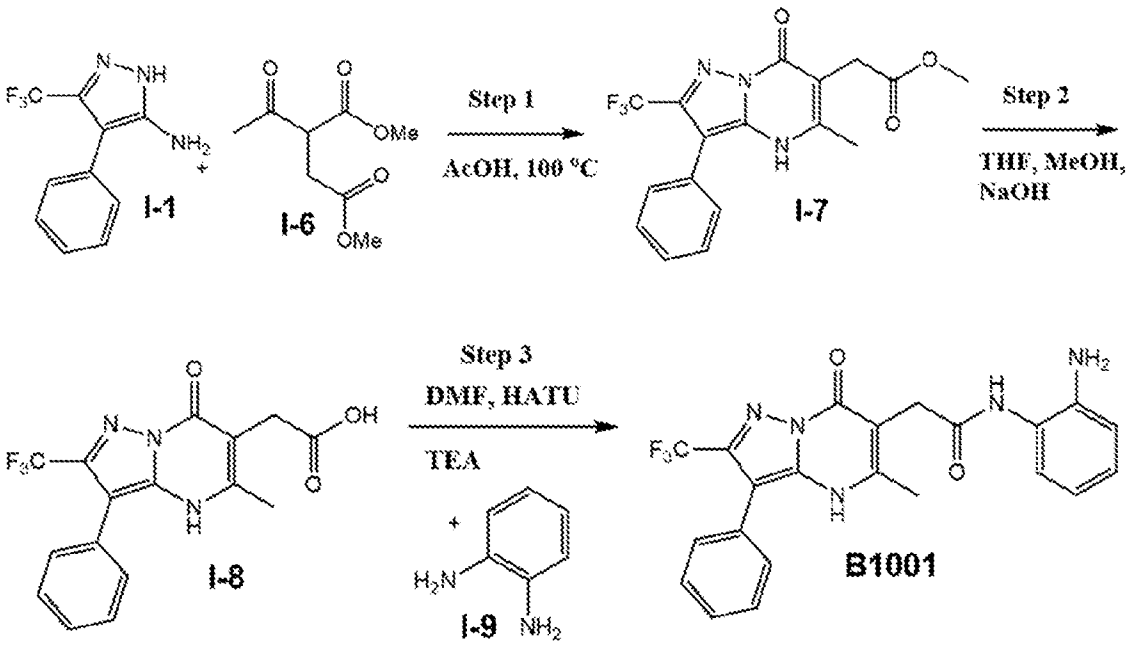
Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1127		(500 MHz, DMSO) δ 8.18 (dd, J = 7.9, 1.5 Hz, 1H), 7.69 (ddd, J = 13.0, 7.9, 6.4 Hz, 2H), 7.64 – 7.60 (m, 1H), 7.51 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.35 (d, J = 7.2 Hz, 1H), 2.45 (s, 3H).	97.0	509.1 (M-H)
A1128		(500 MHz, DMSO) δ 8.43 (t, J = 1.5 Hz, 1H), 8.34 – 8.31 (m, 1H), 8.19 (d, J = 7.8 Hz, 1H), 7.86 (t, J = 7.9 Hz, 1H), 7.49 (d, J = 7.4 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.36 (s, 1H), 2.45 (s, 3H).	94.0	500.1 (M-H)
A1129		(500 MHz, DMSO) δ 12.74 (s, 1H), 10.95 (s, 1H), 7.59 (t, J = 1.7 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.48 – 7.44 (m, 3H), 7.24 (t, J = 2.0 Hz, 1H), 6.90 – 6.87 (m, 1H), 3.78 (s, 3H), 2.51 (s, 3H).	99.4	520.0 and 522.0
A1130		(500 MHz, DMSO) δ 12.98 (s, 1H), 11.57 (s, 1H), 8.44 (d, J = 7.2 Hz, 1H), 7.56 – 7.44 (m, 5H), 7.33 (dd, J = 8.1, 1.3 Hz, 1H), 7.09 (t, J = 8.1 Hz, 1H), 3.88 (s, 3H), 2.76 (s, 3H).	98.7	520.0 and 522.0
A1131		(500 MHz, DMSO) δ 12.99 (s, 1H), 11.42 (s, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.56 – 7.44 (m, 5H), 7.35 (t, J = 8.3 Hz, 1H), 6.90 (dd, J = 8.3, 1.2 Hz, 1H), 3.88 (s, 3H), 2.76 (s, 3H).	99.3	520.0 and 522.0
A1132		(400 MHz, DMSO) δ 7.54 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.35 (d, J = 6.5 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), 6.91 (d, J = 9.7 Hz, 3H), 4.77 (s, 2H), 3.67 (s, 3H), 2.66 (s, 3H).	94.6	519.8 (M-H)
A1133		(500 MHz, DMSO) δ 12.74 (s, 1H), 11.06 (s, 1H), 7.53 – 7.43 (m, 5H), 7.24 (dt, J = 11.2, 1.9 Hz, 1H), 7.06 (s, 1H), 6.56 (dt, J = 10.9, 2.3 Hz, 1H), 3.77 (s, 3H), 2.52 (s, 3H).	96.9	461.2

Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1134		(500 MHz, DMSO) δ 12.74 (s, 1H), 10.95 (s, 1H), 7.55 – 7.49 (m, 2H), 7.49 – 7.44 (m, 4H), 7.21 (t, J = 1.9 Hz, 1H), 6.76 (t, J = 2.0 Hz, 1H), 3.78 (s, 3H), 2.51 (s, 3H).	99.5	477.2
A1135		(500 MHz, DMSO) δ 12.44 – 12.19 (m, 1H), 11.91 (s, 1H), 8.15 – 8.09 (m, 1H), 7.53 – 7.48 (m, 4H), 7.46 – 7.41 (m, 1H), 7.29 (t, *J* = 8.3 Hz, 1H), 6.89 (dd, *J* = 8.4, 1.1 Hz, 1H), 3.88 (s, 3H), 2.74 (s, 3H).	99.4	477.2
A1136		(500 MHz, DMSO) δ 12.91 (s, 1H), 11.35 (s, 1H), 7.88 (t, J = 7.1 Hz, 1H), 7.55 – 7.43 (m, 5H), 7.13 – 7.07 (m, 1H), 6.93 (td, J = 8.3, 1.3 Hz, 1H), 3.86 (s, 3H), 2.68 (s, 3H).	99.6	461.2
A1137		(500 MHz, DMSO) δ 12.97 (s, 1H), 11.75 (s, 1H), 8.26 (d, J = 8.3 Hz, 1H), 7.55 – 7.42 (m, 5H), 7.09 (td, J = 8.4, 6.1 Hz, 1H), 6.97 (ddd, J = 11.0, 8.4, 1.4 Hz, 1H), 3.94 (s, 3H), 2.74 (s, 3H).	99.8	461.2
A1138		(500 MHz, DMSO) δ 12.98 (s, 1H), 11.68 (s, 1H), 8.41 (dd, J = 7.9, 1.7 Hz, 1H), 7.57 – 7.42 (m, 5H), 7.22 – 7.10 (m, 2H), 3.90 (s, 3H), 2.76 (s, 3H).	98.7	477.1
A1139		(500 MHz, DMSO) δ 12.52 (s, 1H), 8.16 – 8.09 (m, 2H), 7.59 – 7.53 (m, 3H), 7.45 – 7.41 (m, 2H), 7.33 – 7.29 (m, 1H), 7.24 (s, 1H), 3.96 – 3.79 (m, 2H), 2.66 (s, 3H), 2.50 (s, 6H).	95.4	548.0 550.0
A1140	NH_3	(500 MHz, DMSO) δ 12.58 (s, 1H), 8.06 (s, 1H), 7.55 – 7.38 (m, 6H), 2.54 (s, 3H).	99	337.6

Compound ID	Compound **I-5** replacement	^{1}H NMR	Purity (%)	MS (m/z)
A1144	 Also replace I-1 with 	(400 MHz, DMSO) δ 11.41 (s, 1H), 7.79 – 7.75 (m, 1H), 7.71 – 7.61 (m, 3H), 7.53 – 7.48 (m, 2H), 7.42 – 7.36 (m, 1H), 6.50 – 6.45 (m, 1H), 3.79 (s, 3H), 2.61 (s, 3H).	95.2	401.2

Example 2

[00415] Synthesis of *N*-(2-aminophenyl)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetamide (**B1001**) was carried out in three steps as follows:



[00416] **Step 1**: Synthesis of methyl 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetate (**I-7**): To a stirred solution of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine (**I-1**, 2.00 g, 8.80 mmol) (WO 2012149157) in AcOH (15 mL) was added dimethyl 2-acetylsuccinate (**I-6**, 1.5 eq, 2.48 g, 13.2 mmol). The reaction mixture was heated at 100 °C for 5 h and concentrated to dryness. The reaction mixture was

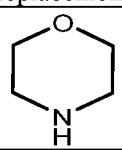
triturated in EtOAc for 15 min. The solid was collected by filtration, rinsed with EtOAc, and dried *in vacuo* to afford compound **I-7** (2.38 g, 6.51 mmol, 74%) as a white solid which was used without further purification. ^{1}H NMR (500 MHz, DMSO) δ 12.27 (s, 1H), 7.56 – 7.39 (m, 5H), 3.63 (s, 3H), 3.61 (s, 2H), 2.34 (s, 3H); MS (m/z): 365.9 $[M+1]^+$, 99.3%.

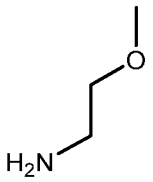
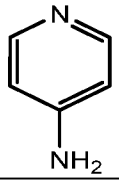
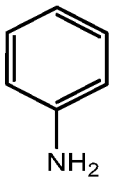
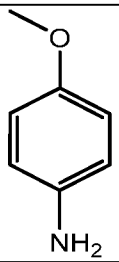
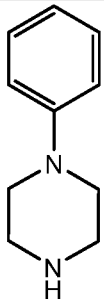
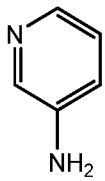
[00417] Step 2: Synthesis of 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetic acid (**I-8**): To a stirred solution of compound **I-7**, 2.38 g, 6.51 mmol) in a mixture of THF (15 mL) and MeOH (15 mL) was added a solution of sodium hydroxide 2M (15 mL, 30 mmol). The reaction mixture was stirred at r.t. for 1.5 h and concentrated to dryness. After addition of water (15 mL) and HCl 10% (15 mL), the white slurry was stirred at r.t. for 15 min. The solid was collected by filtration, rinsed with water, and dried *in vacuo* to afford compound **I-8** (2.27 g, 6.46 mmol, 99%) as a white solid which was used without further purification. MS (m/z): 352.1 $[M+1]^+$, >99%.

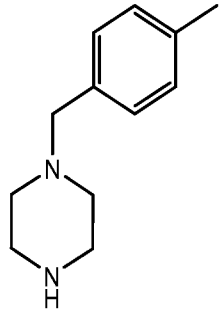
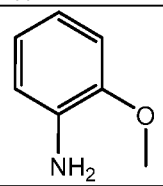
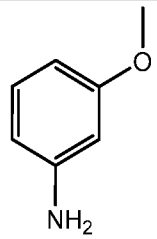
[00418] Step 3: Synthesis of *N*-(2-aminophenyl)-2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetamide (**B1001**): To a stirred solution of compound **I-8** (130 mg, 0.37 mmol) in DMF (1.8 mL) was added HATU (185 mg, 0.48 mmol), o-phenylenediamine (**I-9**, 161 mg, 1.48 mmol) and TEA (104 µL, 0.74 mmol). The reaction mixture was stirred at r.t. for 18h. After addition of EtOAc, water and $NaHCO_3$, the layers were separated and the aqueous layer was extracted with EtOAc. The combined organics layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by reverse flash chromatography (KP-C18-H5, using a gradient 0 to 100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **B1001** (122 mg, 0.27 mmol, 75%) as a beige solid after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 12.24 (s, 1H), 9.20 (s, 1H), 7.53-7.50 (m, 2H), 7.47-7.43 (m, 3H), 7.10 – 7.07 (m, 1H), 6.93 – 6.88 (m, 1H), 6.72 – 6.69 (m, 1H), 6.52 (t, J = 7.0 Hz, 1H), 4.86 (s, 2H), 3.63 (s, 2H), 2.40 (s, 3H); MS (m/z): 442.1 [M+1]+, 99.9%.

[00419] Table 3 below provides additional compounds that can be synthesized similarly to the methods described in Steps 1-3 above, substituting the listed compound for **I-9**. Data for compounds synthesized is provided in columns 3-5.

Table 3

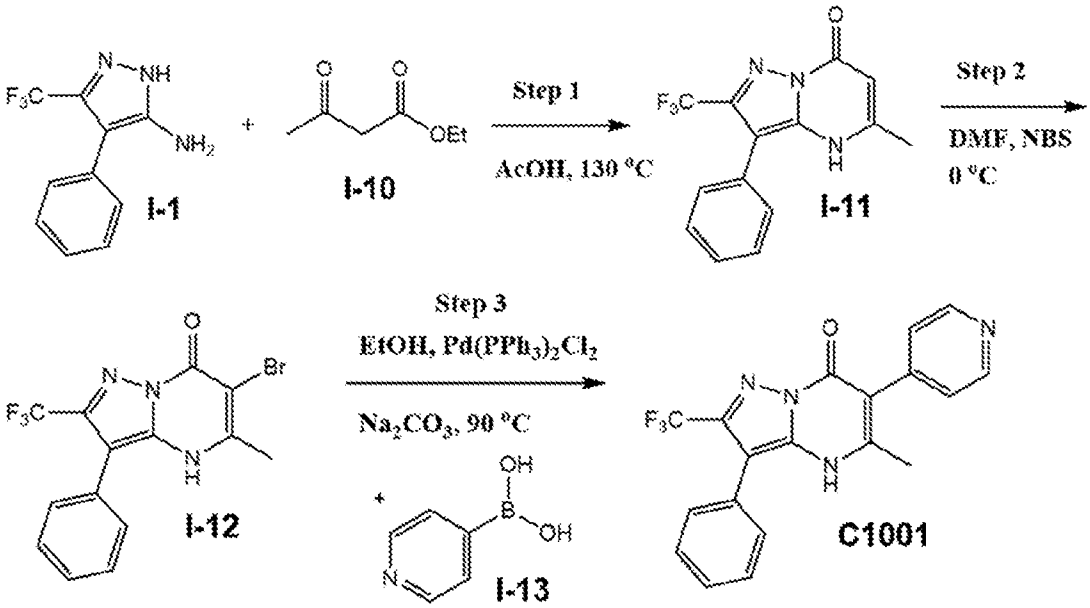
Compound ID	Compound **I-9** replacement	^{1}H NMR	Purity (%)	MS (m/z)
B1002		(500MHz, DMSO) δ 12.22 (s, 1H), 7.58 – 7.34 (m, 5H), 3.64 (s, 4H), 3.62 (s, 2H), 3.58 – 3.52 (m, 2H), 3.48 – 3.41 (m, 2H), 2.28 (s, 3H).	100.0	421.0

Compound ID	Compound **I-9** replacement	^{1}H NMR	Purity (%)	MS (m/z)
B1003		(500MHz, DMSO) δ 12.20 (s, 1H), 7.91 (t, *J* = 5.6Hz, 1H), 7.62 – 7.32 (m, 5H), 3.40 (s, *J* = 15.2Hz, 2H), 3.34 – 3.30 (m, 2H), 3.23 (s, 3H), 3.20 (q, *J* = 5.7Hz, 2H), 2.29 (s, 3H).	100.0	409.0
B1004		(500MHz, DMSO) δ 12.75 (s, 1H), 10.60 (s, 1H), 8.45 (s, 2H), 7.62 (d, *J* = 5.4Hz, 2H), 7.57 – 7.40 (m, 5H), 3.71 (s, 2H), 2.38 (s, 3H).	100.0	428.0
B1005		(500MHz, DMSO) δ 12.27 (s, 1H), 10.06 (s, 1H), 7.59 (dd, *J* = 8.6, 1.0Hz, 2H), 7.52 (dd, *J* = 11.2, 4.4Hz, 2H), 7.49 – 7.42 (m, 3H), 7.33 – 7.26 (m, 2H), 7.03 (t, *J* = 7.4Hz, 1H), 3.65 (s, 2H), 2.37 (s, 3H).	100.0	427.0
B1006		(500MHz, DMSO) δ 12.25 (s, 1H), 9.89 (s, 1H), 7.58 – 7.39 (m, 7H), 6.96 – 6.80 (m, 2H), 3.71 (s, 3H), 3.62 (s, 2H), 2.37 (s, 3H).	99.7	457.0
B1007		(500MHz, DMSO) δ 12.22 (s, 1H), 7.54 – 7.41 (m, 5H), 7.24 (dd, *J* = 8.7, 7.3Hz, 2H), 6.98 (d, *J* = 7.9Hz, 2H), 6.82 (t, *J* = 7.3Hz, 1H), 3.84 – 3.75 (m, 2H), 3.68 (s, 2H), 3.65 – 3.57 (m, 2H), 3.27 – 3.20 (m, 2H), 3.15 – 3.07 (m, 2H), 2.30 (s, 3H).	98.1	496.1
B1008		(500MHz, DMSO) δ 12.29 (s, 1H), 10.28 (s, 1H), 8.75 (d, *J* = 2.2Hz, 1H), 8.26 (d, *J* = 3.6Hz, 1H), 8.02 (ddd, *J* = 8.4, 2.5, 1.5Hz, 1H), 7.55 – 7.40 (m, 5H), 7.34 (dd, *J* = 8.2, 4.5Hz, 1H), 3.69 (s, 2H), 2.38 (s, 3H).	99.1	428.0

Compound ID	Compound **I-9** replacement	^{1}H NMR	Purity (%)	MS (m/z)
B1009		(500MHz, DMSO) δ 12.21 (s, 1H), 7.54 – 7.40 (m, 5H), 7.25 – 7.10 (m, 4H), 3.67 – 3.56 (m, 4H), 3.52 – 3.38 (m, 4H), 2.46 – 2.38 (m, 2H), 2.37 – 2.30 (m, 2H), 2.29 (s, 3H), 2.26 (s, 3H).	96.1	524.1
B1010		(400MHz, DMSO) δ 12.26 (s, 1H), 9.22 (s, 1H), 7.91 (d, J = 7.9Hz, 1H), 7.55 – 7.40 (m, 5H), 7.10 – 7.00 (m, 2H), 6.92 – 6.84 (m, 1H), 3.84 (s, 3H), 3.71 (s, 2H), 2.39 (s, 3H).	99.2	457.0
B1011		(400MHz, DMSO) δ 12.28 (s, 1H), 10.07 (s, 1H), 7.55 – 7.48 (m, 2H), 7.46 (t, J = 6.5Hz, 3H), 7.32 (s, 1H), 7.20 (t, J = 8.1Hz, 1H), 7.11 (d, J = 8.3Hz, 1H), 6.62 (dd, J = 8.1, 1.9Hz, 1H), 3.71 (s, 3H), 3.64 (s, 2H), 2.37 (s, 3H).	99.7	457.0

Example 3

[00420] Synthesis of 5-methyl-3-phenyl-6-(pyridin-4-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1001**) was carried out in three steps as follows:



[00421] **Step 1**: Synthesis of 5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-11**): To a stirred solution of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine

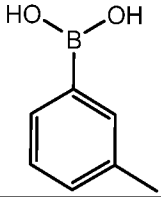
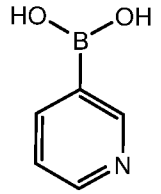
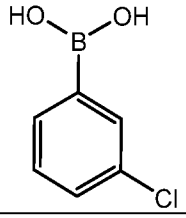
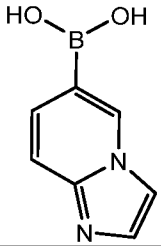
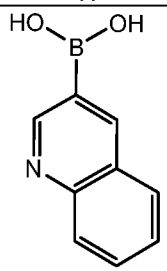
(**I-1**, 1.43 g, 6.29mmol) (WO 2012149157) in AcOH (31.5 mL) was added ethyl acetoacetate (**I-10**, 1 eq, 796 µL, 6.29 mmol). The reaction mixture was heated at 130 °C for 1 h and concentrated to dryness. The reaction mixture was triturated in EtOAc for 15 min. The solid was collected by filtration, rinsed with EtOAc, and dried *in vacuo* to afford compound **I-11** (1.04g, 6.29 mmol, 56%) as a white solid which was used without further purification. ^{1}H NMR (500 MHz, DMSO) δ 12.27 (s, 1H), 7.52 – 7.44 (m, 3H), 7.43 – 6.7.40 (m, 2H), 5.79 (d, J = 0.6 Hz, 1H), 2.30 (s, 3H); MS (m/z): 294.1 [M+1]+, 99.9%.

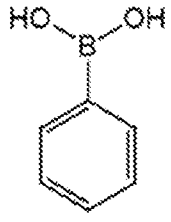
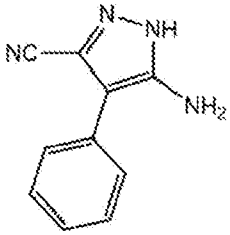
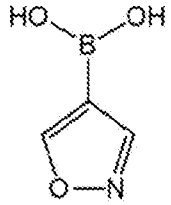
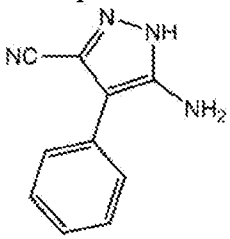
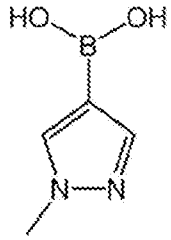
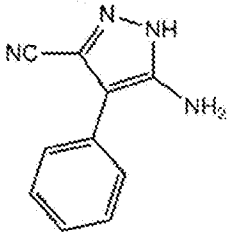
[00422] Step 2: Synthesis of 6-bromo-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-12**): To a stirred suspension of compound **I-11** (830 mg, 2.83 mmol) in DMF (9.4 mL) was added *N*-bromosuccinimide (509 mg, 2.83 mmol) at 0 °C. The reaction mixture was stirred at r.t. for 30 min. After addition of water, the white slurry was stirred at r.t. for 10 min. The solid was collected by filtration, rinsed with water, and dried *in vacuo* to afford compound **I-12** (921 mg, 2.47 mmol, 87%) as an off-white solid which was used without further purification. MS (m/z): 372.2-374.2 [M+1]+, 98.1%.

[00423] Step 3: Synthesis of 5-methyl-3-phenyl-6-(pyridin-4-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1001**): To a stirred solution of compound **I-12** (100 mg, 0.26 mmol) in a mixture of degassed EtOH (4 mL) and water (1 mL) was added pyridine-4-boronic acid (**I-13**, 40 mg, 0.32 mmol), $Pd(PPh_3)_2Cl_2$ (19 mg, 0.02 mmol) and Na_2CO_3 (117 mg, 1.10 mmol). The reaction mixture was heated at 90 °C for 18h. The reaction mixture was filtered through Celite, washed with MeOH and concentrated *in vacuo*. The residue was purified twice by reverse flash chromatography (KP-C18- H5, using a gradient 0 to 100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **C1001** (7.4 mg, 0.02 mmol, 7%) as a yellow solid after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 12.61 (bs, 1H), 8.62 (s, 2H), 7.52 – 7.48 (m, 4H), 7.45 – 7.39 (m, 3H), 2.21 (s, 3H); MS (m/z): 371.2 $[M+1]^+$, 98.7%.

[00424] Table 4 below provides additional compounds that can be synthesized similarly to the methods described in Steps 1-3 above, substituting the listed compound for **I-13**. Data for compounds synthesized is provided in columns 3-5.

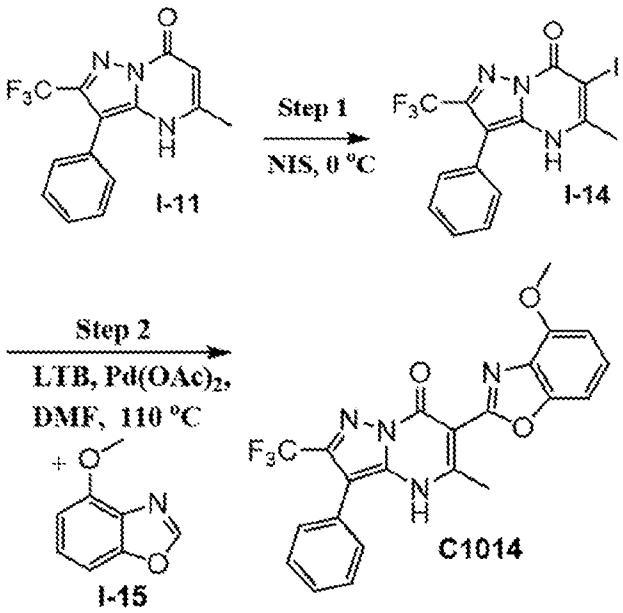
Table 4

Compound ID	Compound **I-13** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1002		(500MHz, DMSO) δ 12.35 (s, 1H), 7.53-7.44 (m, 5H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.13 – 7.08 (m, 2H), 2.35 (s, 3H), 2.15 (s, 3H).	95.7	384.2
C1003		(500MHz, DMSO) δ 12.50 (bs, 1H), 8.56 (d, *J* = 10.9 Hz, 2H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.45 (m, 6H), 2.21 (s, 3H).	99.2	371.0
C1004		(500MHz, DMSO) δ 12.43 (s, 1H), 7.54 – 7.40 (m, 8H), 7.31 (dt, *J* = 7.4, 1.4 Hz, 1H), 2.18 (s, 3H).	98.7	404.1
C1006		(500MHz, DMSO) δ 8.53 (s, 1H), 7.99 (s, 1H), 7.66-7.61 (m, 2H), 7.52 – 7.47 (m, 4H), 7.44-7.40 (m, 1H), 7.21 (dd, J = 9.2, 1.4 Hz, 1H), 2.23 (s, 3H).	98.4	410.2
C1007		(500MHz, DMSO) δ 12.57 (bs, 1H), 8.86 (s, 1H), 8.34 (d, J = 1.5 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 7.8 Hz, 1H), 7.83 – 7.77 (m, 1H), 7.65 (t, J = 7.4 Hz, 1H), 7.55 – 7.44 (m, 5H), 2.27 (s, 3H).	99.9	421.1

Compound ID	Compound **I-13** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1273	 Also replace **I-1** with 	(400 MHz, DMSO) δ 12.56 (s, 1H), 7.64 – 7.56 (m, 4H), 7.53 – 7.43 (m, 3H), 7.42 – 7.36 (m, 1H), 7.36 – 7.31 (m, 2H), 2.22 (s, 3H).	95.9	327.1
C1281	 Also replace **I-1** with 	(500 MHz, DMSO): δ 9.17 (s, 1H), 8.86 (s, 1H), 7.67 (d, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.7 Hz, 2H), 7.53 – 7.42 (m, 1H), 2.46 (s, 3H).	100	318.1
C1282	 Also replace **I-1** with 	(500 MHz, DMSO) δ 7.88 (s, 1H), 7.86 – 7.73 (m, 2H), 7.58 (s, 1H), 7.53-7.50 (m., 2H), 7.38 (s, 1H), 3.88 (s, 3H), 2.40 (s, 3H).	100	329.1 (M-H)

Example 4

[00425] Synthesis of 6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1014**) was carried out in two steps as follows:



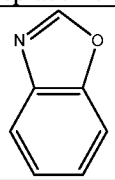
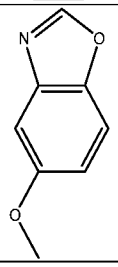
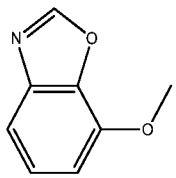
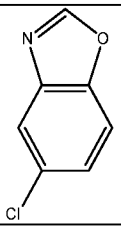
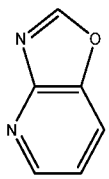
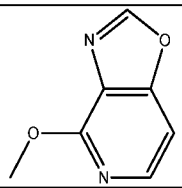
[00426] **Step 1**: Synthesis of 6-iodo-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-14**): To a suspension of 5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-11**, 450 mg, 1.53 mmol) was added *N*-iodosuccinimide (363 mg, 1.53 mmol) at 0 °C. After 30 min, LCMS showed complete conversion. The reaction was poured into water. The precipitated solid was filtered, washed with dilute aquoues $Na_2S_2O_3$ followed by water. The solid was dried under high vacuum to afford the desired **I-14**. ^{1}H NMR (500 MHz, DMSO) δ 12.75 (bs, 1H), 7.53 – 7.40 (m, 5H), 2.58 (s, 3H). MS (m/z): 420.0 $[M+1]^+$.

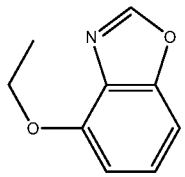
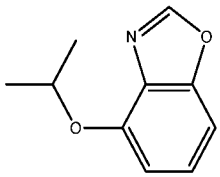
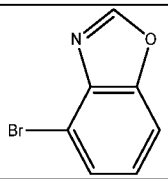
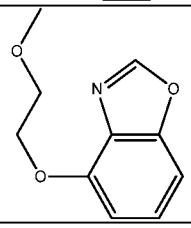
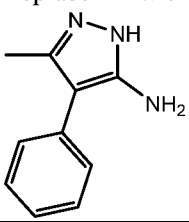
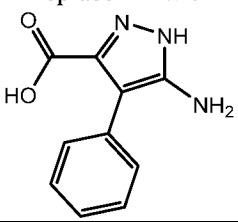
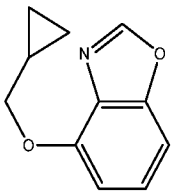
[00427] **Step 2**: Synthesis of 6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1014**): A mixture of 6-iodo-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4H)-one (**I-14,**100 mg, 239 µmol), 4-methoxybenzo[d]oxazole (**I-15**, 53.5 mg, 358 µmol), Lithium *tert*-butoxide (133 µL, 1.43 mmol) and palladium(ll) acetate (5.36 mg, 23.9 µmol) in DMF (1.50 mL) was degased with nitrogen. The reaction mixture was heated at 110 °C for 16 h. The crude reaction mixture was filtered over celite and washed with ethyl acetate. The filtrate was evaporated and the residue was purified by reverse phase column chromatography using a gradient of 20-70% MeCN/H2O (0.1% ammonium formate buffer) to give compound **C1014**

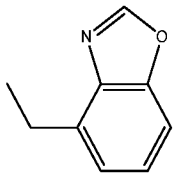
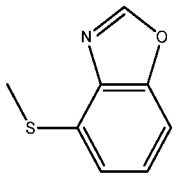
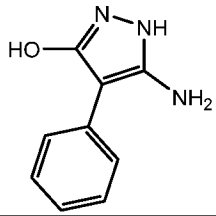
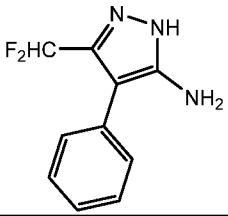
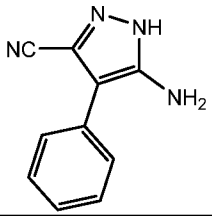
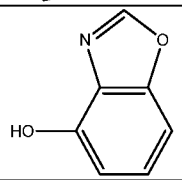
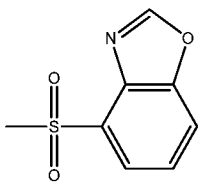
(96.9% purity). ^{1}H NMR (500 MHz, DMSO) δ 12.95 (s, 1H), 7.52-7.43 (m, 5H), 7.35 (d, J = 4.6 Hz, 2H), 7.01 – 6.91 (m, 1H), 4.00 (s, 3H), 2.48 (s, 3H). MS (m/z): 441.2 $[M+1]^+$.

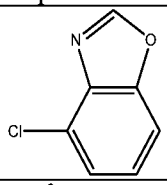
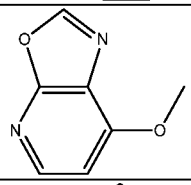
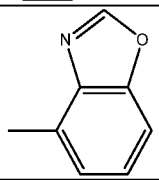
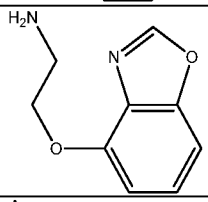
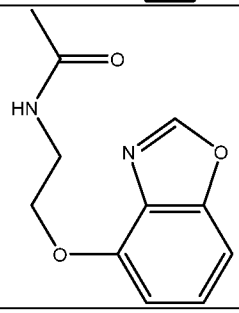
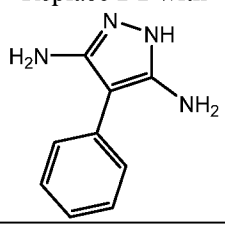
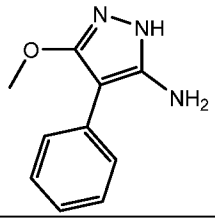
[00428] Table 5 below provides additional compounds that can be synthesized similarly to the methods described in Steps 1-2 above, optionally substituting the listed compound as indicated for **I-15**, and/or substituting for **I-1** and/or **I-10** where indicated to provide the suitable analog of **I-11** (per Example 3). Data for compounds synthesized is provided in columns 3-5.

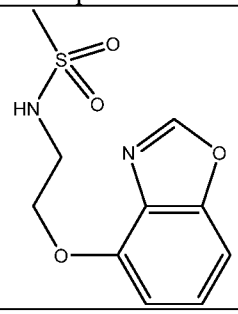
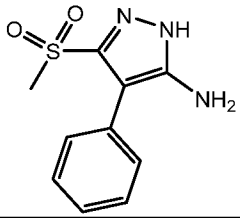
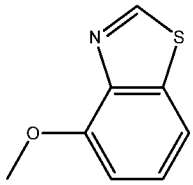
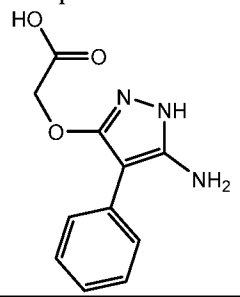
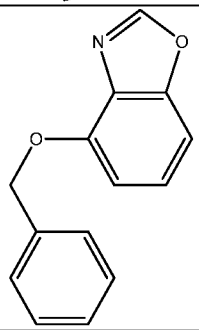
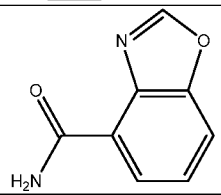
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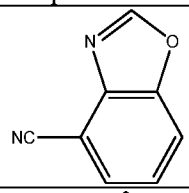
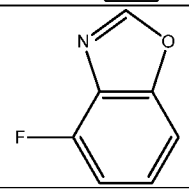
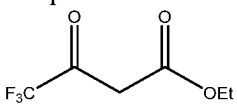
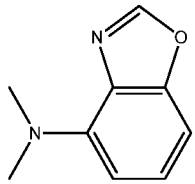
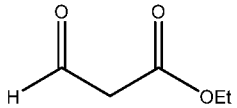
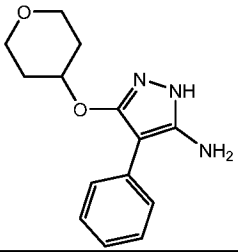
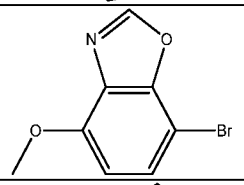
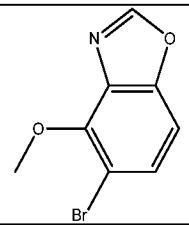
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1011		(500 MHz, DMSO) δ 12.96 (s, 1H), 7.66 (d, J = 8.7 Hz, 1H), 7.57 – 7.28 (m, 6H), 7.03 – 6.98 (m, 1H), 3.84 (s, 3H), 2.44 (s, 3H).	95.1	411.1
C1012		(500 MHz, DMSO) δ 12.96 (s, 1H), 7.66 (d, J = 8.7 Hz, 1H), 7.57 – 7.28 (m, 6H), 7.03 – 6.98 (m, 1H), 3.84 (s, 3H).	97.0	441.2
C1022		(500 MHz, DMSO) δ 7.59 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 7.3 Hz, 2H), 7.28 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 8.1 Hz, 1H), 3.99 (s, 3H), 2.38 (s, 3H).	96.4	441.2
C1028		(500 MHz, MeOD) δ 7.77 (s, 1H), 7.66 (sb, 1H), 7.52 – 7.40 (m, 6H), 2.59 (s, 3H).	95.3	445.0
C1030		(500 MHz, DMSO, Aromatic protons only) δ 8.45 (dd, J = 4.9, 1.4 Hz, 1H), 8.12 (dd, J = 8.0, 1.4 Hz, 1H), 7.60 (d, J = 7.7 Hz, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.37 – 7.28 (m, 2H).	97.7	412.2
C1037		(500 MHz, DMSO) δ 8.01 (d, J = 5.7 Hz, 1H), 7.49 (d, J = 13.6 Hz, 2H), 7.42 – 7.33 (m, 3H), 7.29 – 7.23 (m, 1H), 3.99 (s, 3H), 2.35 (s, 3H).	96.4	442.2

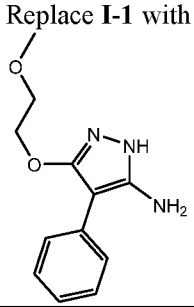
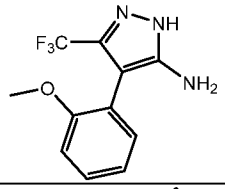
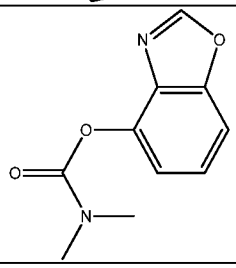
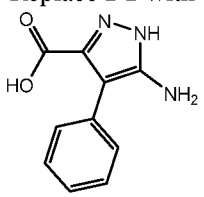
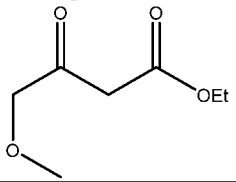
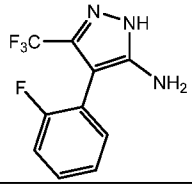
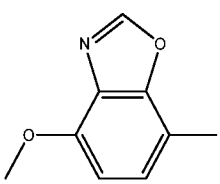
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1038		(500 MHz, DMSO) δ 8.27 (s, 1H), 7.60 (d, J = 7.3 Hz, 2H), 7.46 – 7.38 (m, 2H), 7.33 – 7.17 (m, 3H), 6.91 – 6.83 (m, 1H), 4.35 (q, J = 7.0 Hz, 2H), 2.35 (s, 3H), 1.42 (t, J = 7.0 Hz, 3H).	99.2	455.2
C1039		(500 MHz, DMSO) δ 12.71 (s, 1H), 8.13 (s, 1H), 7.59 (d, J = 7.5 Hz, 2H), 7.44 (dd, J = 10.6, 4.8 Hz, 2H), 7.31 (t, J = 7.4 Hz, 1H), 7.27 – 7.21 (m, 2H), 6.87 (dd, J = 7.5, 1.5 Hz, 1H), 5.23 – 5.06 (m, 1H), 2.38 (s, 3H), 1.36 (d, J = 6.1 Hz, 6H).	99.3	469.1
C1040		(500 MHz, DMSO) δ 8.08 (s, 1H), 7.71 (dd, J = 8.1, 0.8 Hz, 1H), 7.60 – 7.54 (m, 3H), 7.44 – 7.40 (m, 2H), 7.31 – 7.26 (m, 2H), 2.44 (s, 3H).	99.4	488.0 and 490.0
C1041		(500 MHz, DMSO) δ 7.60 (d, J = 7.4 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.31 – 7.21 (m, 3H), 6.89 (d, J = 8.9 Hz, 1H), 4.47 – 4.41 (m, 2H), 3.78 – 3.72 (m, 2H), 3.34 (s, 3H), 2.35 (s, 3H).	98.2	485.3
C1042	Replace **I-1** with 	(500 MHz, DMSO) δ 12.47 (brs, 1H), 7.52 (d, J = 4.5 Hz, 4H), 7.44 – 7.29 (m, 3H), 6.97 (dd, J = 7.0, 2.0 Hz, 1H), 4.01 (s, 3H), 2.48 (S, 3H), 2.33 (s, 3H).	99.5	387.8
C1043	Replace **I-1** with 	(500 MHz, DMSO) δ 7.58 (d, J = 7.0 Hz, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.32 – 7.26 (m, 3H), 6.94 – 6.89 (m, 1H), 4.00 (s, 3H), 2.43 (s, 3H).	98.0	417.3
C1045		(500 MHz, DMSO) δ 7.60 (d, J = 7.7 Hz, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.30 – 7.20 (m, 3H), 6.86 (d, J = 7.8 Hz, 1H), 4.14 (d, J = 7.0 Hz, 2H), 2.35 (s, 3H), 1.33 (m, 1H), 0.60 (q, J = 5.5 Hz, 2H), 0.38 (t, J = 4.9 Hz, 2H).	98.9	481.2

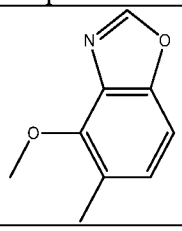
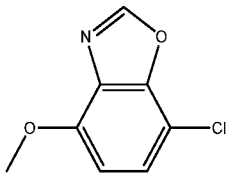
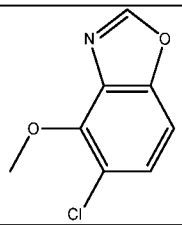
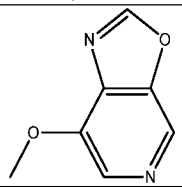
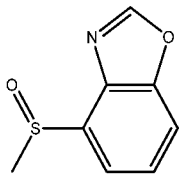
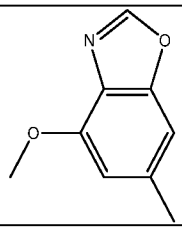
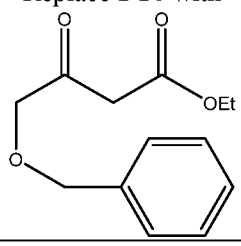
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1046		(500 MHz, DMSO) δ 12.96 (brs, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.52 (m, 4H), 7.46 (dd, J = 8.9, 4.4 Hz, 1H), 7.40 – 7.31 (m, 1H), 7.24 (d, J = 7.3 Hz, 1H), 2.99 (q, J = 7.6 Hz, 2H), 1.34 (t, J = 7.6 Hz, 3H).	98.7	439.1
C1047		(500 MHz, DMSO) δ 7.60 (d, J = 7.3 Hz, 2H), 7.48 (dd, J = 8.1, 0.8 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.32 – 7.27 (m, 2H), 7.17 (dd, J = 7.8, 0.8 Hz, 1H), 2.62 (s, 3H), 2.40 (s, 3H).	94.8	457.1
C1049	Replace **I-1** with 	(500 MHz, DMSO) δ 11.73 – 11.39 (m, 1H), 8.50-8.20 (s, 2H), 7.34-7.19 (m, 4H), 7.01 (s, 1H), 6.89 (t, J = 4.5 Hz, 1H), 4.00 (s, 3H), 2.45 (s, 3H)	100	389.2
C1050	Replace **I-1** with 	(500 MHz, DMSO) δ 7.75 (dd, J = 8.3, 1.2 Hz, 2H), 7.36 – 7.30 (m, 2H), 7.22 – 7.12 (m, 3H), 7.06 – 6.92 (m, J = 53.9 Hz, 1H), 6.82 (dd, J = 6.8, 2.2 Hz, 1H), 3.93 (s, 3H), 2.33 (s, 3H).	97.6	423.1
C1051	Replace **I-1** with 	(DMSO, 500 MHz) δ 8.08 (dd, J = 8.3, 1.1 Hz, 2H), 7.49 (dd, J = 10.7, 5.0 Hz, 2H), 7.35 – 7.22 (m, 3H), 6.91 (dd, J = 5.1, 3.9 Hz, 1H), 4.01 (s, 3H), 2.45 (s, 3H).	99.9	398.1
C1053		(500 MHz, DMSO) δ 7.60 (d, J = 7.3 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.30 – 7.26 (m, 1H), 7.15 – 7.07 (m, 2H), 6.71 (dd, J = 7.6, 1.4 Hz, 1H), 2.32 (s, 3H).	96.7	427.2
C1054		(500 MHz, DMSO) δ 8.42 (s, 2H), 8.08 (dd, J = 8.1, 1.0 Hz, 1H), 7.78 (dd, J = 7.8, 1.0 Hz, 1H), 7.60 (s, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.33 – 7.27 (m, 1H), 3.51 (s, 3H), 2.57 (s, 1.5H), 2.54 (s, 1.5H).	97.5	489.2

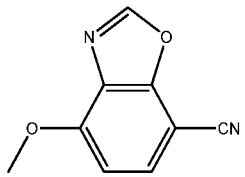
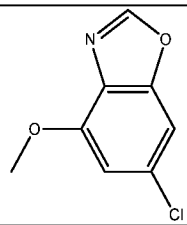
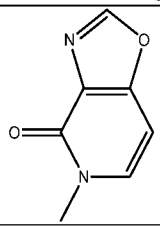
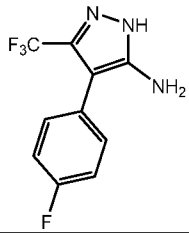
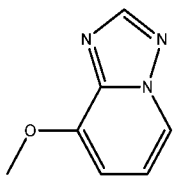
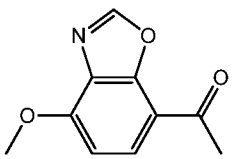
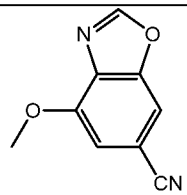
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1055		(500 MHz, DMSO) δ 13.02 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 7.5 Hz, 2H), 7.48 (t, J = 7.7 Hz, 3H), 7.42 – 7.36 (m, 2H), 2.50 (s, 3H).	96.0	441.2
C1058		(500 MHz, DMSO) δ 8.11 (d, J = 5.6 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.51 – 7.43 (m, 3H), 7.42 – 7.34 (m, 1H), 4.07 (s, 3H), 2.46 (s, 3H).	95.0	442.1
C1060		(500 MHz, DMSO) δ 12.96 (s, 1H), 7.58 – 7.48 (m, 5H), 7.45 – 7.39 (m, 1H), 7.30 (t, J = 7.8 Hz, 1H), 7.24 – 7.18 (m, 1H), 2.58 (s, 3H), 2.47 (s, 3H).	99.7	425.2
C1061		(400 MHz, DMSO) δ 8.00 (s, 3H), 7.53 – 7.23 (m, 7H), 6.96 (s, 1H), 4.51 (m, 2H), 2.62 (s, 3H).	94.6	470.0
C1062		(400 MHz, DMSO) δ 8.20 (s, 2H), 7.60 (m, 2H), 7.45 – 7.38 (m, 2H), 7.28 (m, 3H), 6.90 (m, 1H), 4.32 (m, 2H), 2.35 (s, 3H), 1.84 (s, 3H).	93.5	512.0
C1063	Replace **I-1** with 	(500 MHz, DMSO) δ 12.10 (brs, 1H), 7.65-7.53 (m, 2H), 7.50-7.43 (m, 2H), 6.94 (d, J = 6.9 Hz, 1H), 5.35 (brs, 2H), 4.00 (s, 3H), 2.80 (s, 3H).	100	388.6
C1064	Replace **I-1** with 	(500 MHz, DMSO) δ 12.40 (s, 1H), 7.54-7.22 (m, 7H), 6.91-6.87 (m, 1H), 4.02 (s, 3H), 4.01 (s, 3H), 2.44 (s, 3H).	95.5	403.1

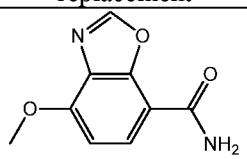
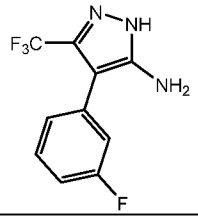
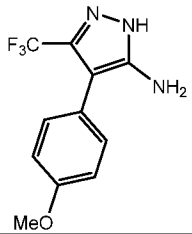
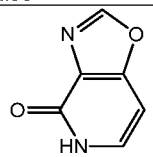
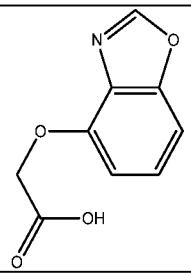
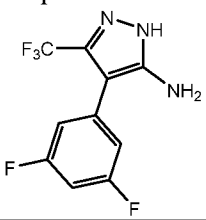
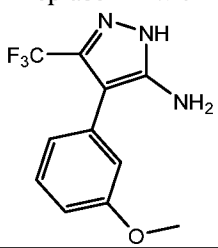
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1066		(500 MHz, DMSO) δ 8.26 (s, 1H), 7.60 (d, J = 7.3 Hz, 2H), 7.45 – 7.39 (m, 2H), 7.31 – 7.22 (m, 3H), 6.91 (dd, J = 8.0, 1.0 Hz, 1H), 4.36 (t, J = 5.6 Hz, 2H), 3.02 (s, 3H), 2.36 (s, 3H).	96.2	548.1
C1068	Replace **I-1** with 	(500 MHz, DMSO) δ 12.92 (brs, 1H), 7.67 (m, 2H), 7.51-7.46 (m, 2H), 7.44-7.38 (m, 1H), 7.37-7.33 (m, 2H), 6.98-6.95 (m, 1H), 4.01 (s, 3H), 2.47 (s, 3H).	100	451.1
C1070		(500 MHz, DMSO) δ 7.63 (d, J = 7.3 Hz, 2H), 7.55 (dd, J = 7.9, 0.9 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.33 – 7.27 (m, 2H), 7.20 (t, J = 7.9 Hz, 1H), 6.94 (dd, J = 7.9, 0.8 Hz, 1H), 3.99 (s, 3H), 2.94 (s, 3H).	95.4	457.1
C1072	Replace **I-1** with 	(400 MHz, DMSO) δ 8.57 (d, J = 7.8 Hz, 2H), 7.28-7.21 (m, 4H), 6.96 (t, J = 7.1 Hz, 1H), 6.90 – 6.85 (m, 1H), 4.94 (s, 2H), 3.99 (s, 3H), 2.42 (s, 3H).	96.4	447.1
C1073		(500 MHz, DMSO) δ 12.96 (s, 1H), 7.54 – 7.50 (m, 6H), 7.44 – 7.40 (m, 3H), 7.37 – 7.34 (m, 3H), 7.05 (d, J = 8.8 Hz, 1H), 5.42 (s, 2H), 2.48 (s, 3H).	94.4	517.2
C1074		(500 MHz, DMSO) δ 8.64 (s, 1H), 7.94 – 7.90 (m, 1H), 7.86 (s, 1H), 7.61 (s, 1H), 7.60 (s, 1H), 7.46 – 7.40 (m, 4H), 7.33 – 7.29 (m, 2H), 2.55 (s, 3H).	96.0	454.2

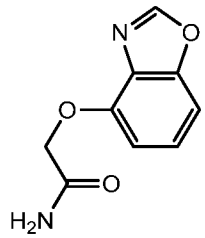
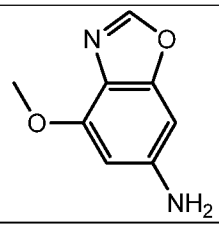
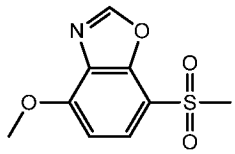
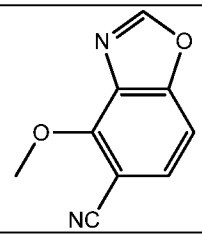
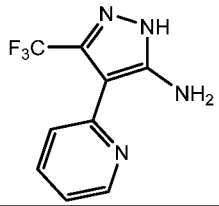
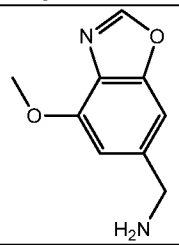
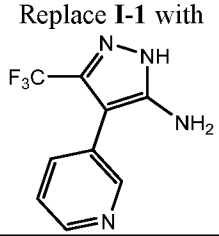
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1075		(500 MHz, DMSO) δ 8.07 (dd, J = 8.1, 0.9 Hz, 1H), 7.80 (dd, J = 7.8, 0.9 Hz, 1H), 7.61 (s, 1H), 7.59 (s, 1H), 7.49 – 7.41 (m, 3H), 7.38 – 7.28 (m, 2H), 2.55 (s, 3H).	94.0	436.2 (M-H)
C1076		(500 MHz, DMSO) δ 13.02 (s, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.55 – 7.44 (m, 6H), 7.32 – 7.27 (m, 1H), 2.55 (s, 3H).	97.9	429.7
C1077	Replace **I-10** with 	(500 MHz, DMSO) δ 7.60 (d, J = 7.4 Hz, 2H), 7.47 (t, J = 7.7 Hz, 2H), 7.38 – 7.29 (m, 3H), 6.94 (dd, J = 7.8, 1.1 Hz, 1H), 3.99 (s, 3H).	97.3	495.1
C1078		(400 MHz, DMSO) δ 7.50-7.41 (m, 4H), 7.41 (t, J = 7.0 Hz, 1H), 7.20 (t, J = 8.1 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 6.56 (d, J = 8.2 Hz, 1H), 3.19 (s, 6H), 2.46 (s, 3H).	97.9	454.2
C1079	Replace **I-10** with 	(400 MHz, DMSO) δ 8.71 (s, 1H), 7.59 (d, J = 6.3 Hz, 2H), 7.44 m, 2H), 7.29 (m, 2H), 7.19 (d, J = 5.6 Hz, 1H), 6.87 (d, J = 7.9 Hz, 1H), 3.98 (s, 3H).	99.3	427.1
C1080	Replace **I-1** with 	(500 MHz, DMSO) δ 8.53 (dd, J = 8.5, 1.3 Hz, 2H), 8.24 (s, 1H), 7.27 – 7.21 (m, 4H), 7.00 – 6.94 (m, 1H), 6.88 (dd, J = 6.9, 2.1 Hz, 1H), 4.88 – 4.81 (m, 1H), 3.99 (s, 3H), 3.91 (dd, J = 11.1, 4.4 Hz, 2H), 2.41 (s, 3H), 1.55 (d, J = 9.1 Hz, 2H).	100	473.3
C1081		(500 MHz, DMSO) δ 12.72 (s, 1H), 7.60-7.54 (m, 2H), 7.53-7.43 (m, 3H), 7.39-7.33 (m, 1H), 6.93 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H), 2.42 (s, 3H).	96.1	518.9 520.6
C1082		(400 MHz, DMSO) δ 13.08 – 12.91 (m, 1H), 7.57 – 7.52 (m, 3H), 7.51-7.45 (m, 2H), 7.43-7.39 (m, 1H), 7.37 (d, J = 8.6 Hz, 1H), 4.37 (s, 3H), 2.52 (s, 3H).	100	519.0 521.1

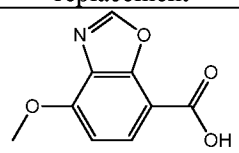
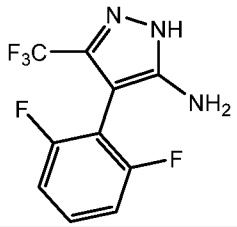
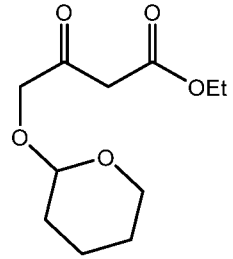
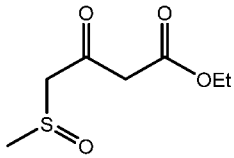
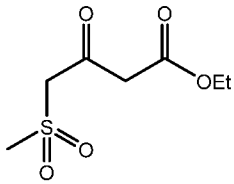
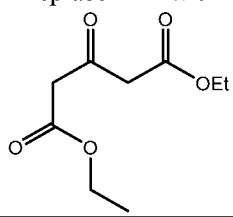
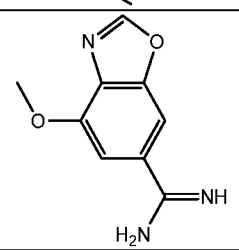
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1083	Replace **I-1** with 	(500 MHz, DMSO) δ 12.72 (s, 1H), 8.63 – 8.35 (m, 2H), 7.36-7.21 (m, 4H), 7.09 – 6.94 (m, 1H), 6.94-6.88 (m, 1H), 4.36 (t, J = 5.9 Hz, 2H), 3.99 (s, 3H), 3.48-3.43 (m, 2H), 3.16 (s, 3H), 2.43 (s, 3H).	96.5	447.1
C1086	Replace **I-1** with 	(500 MHz, DMSO) δ 12.82 (brs, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.41 – 7.32 (m, 3H), 7.17 (d, J = 8.3 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.98 (dd, J = 6.6, 2.3 Hz, 1H), 4.01 (s, 3H), 3.78 (s, 3H).	99.8	471.1
C1088		(500 MHz, DMSO) δ 12.87 (d, J = 132.8 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.57 (s, 1H), 7.56 (s, 1H), 7.51 – 7.45 (m, 2H), 7.41 – 7.35 (m, 2H), 7.15 (d, J = 8.0 Hz, 1H), 3.15 (s, 3H), 2.96 (s, 3H), 2.43 (s, 3H).	99.9	498.2
C1090	Replace **I-1** with  And replace **I-10** with 	(500 MHz, DMSO) δ 12.83 (s, 1H), 7.63 (d, J = 7.1 Hz, 7H), 7.39 (t, J = 7.7 Hz, 7H), 7.31 – 7.24 (m, J = 9.1, 5.4 Hz, 10H), 6.91 (dd, J = 6.3, 2.6 Hz, 4H), 4.53 (s, 7H), 4.01 (s, 10H), 3.09 (s, 10H).	100	447.0
C1091	Replace **I-1** with 	(500 MHz, DMSO) δ 13.09 (brs, 1H), 7.58–7.50 (m, 2H), 7.40–7.32 (m, 4H), 6.98–6.96 (m, 1H), 4.01 (s, 3H), 2.48 (s, 3H).	99.9	459.1
C1092		(500 MHz, DMSO) δ 12.77 (s, 1H), 7.56 (d, J = 7.5 Hz, 2H), 7.46 (t, J = 7.7 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.10 (d, J = 8.3 Hz, 1H), 6.82 (d, J = 8.2 Hz, 1H), 3.96 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H).	98.7	455.2

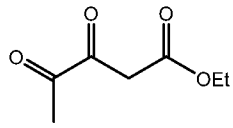
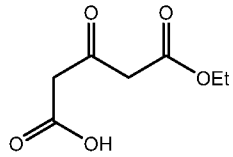
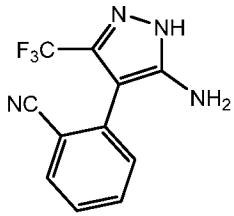
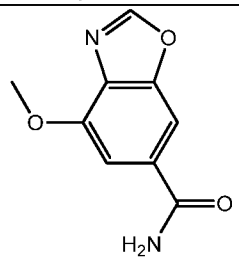
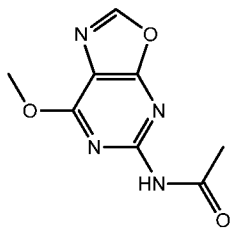
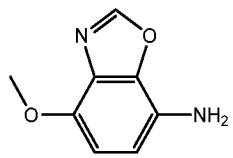
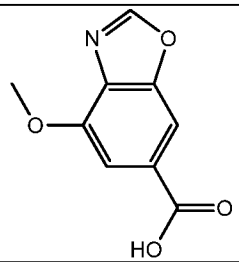
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1093		(500 MHz, DMSO) δ 12.74 (s, 1H), 7.59 (d, J = 7.1 Hz, 2H), 7.44 (t, J = 7.3 Hz, 2H), 7.31 (m, 1H), 7.21 (d, J = 8.1 Hz, 1H), 7.12 (d, J = 8.1 Hz, 1H), 4.31 (s, 3H), 2.42 (s, 3H), 2.27 (s, 3H).	97.1	455.2
C1094		(500 MHz, DMSO) δ 7.60 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.35 (d, J = 8.7 Hz, 1H), 7.29 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 8.8 Hz, 1H), 4.00 (s, 3H), 2.37 (s, 3H).	98.9	475.1
C1095		(500 MHz, DMSO) δ 7.59 (d, J = 7.4 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.35 (s, 2H), 7.29 (t, J = 7.4 Hz, 1H), 4.37 (s, 3H), 2.45 (s, 3H).	98.2	475.1
C1096		(500 MHz, DMSO) δ 8.75 (s, 1H), 8.27 (s, 1H), 7.59 – 7.52 (m, 2H), 7.51 – 7.44 (m, 2H), 7.42 – 7.35 (m, 1H), 4.15 (s, 3H), 2.55 (s, 3H).	95.3	442.0
C1097		(500 MHz, DMSO) δ 7.88 (dd, J = 8.0, 0.9 Hz, 1H), 7.64 (dd, J = 7.7, 1.0 Hz, 1H), 7.61 – 7.54 (m, 3H), 7.43 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 2.99 (s, 3H), 2.47 (s, 3H).	99.8	473.0
C1098		(500 MHz, DMSO) δ 7.55–7.48 (m, 5H), 7.17 (s, 1H), 6.81 (s, 1H), 3.98 (s, 3H), 2.48 (s, 3H), 2.46 (s, 3H)	99.6	455.0
C1099	Replace **I-10** with 	(500 MHz, DMSO) δ 7.52-7.50 (m, 5H), 7.36-7.34 (m, 3H), 7.18 – 7.12 (m, 2H), 7.03 (d, J = 6.3 Hz, 2H), 6.96 (m, 1H), 4.70 (s, 2H), 4.36 (s, 2H), 4.01 (s, 3H).	94.8	547.1

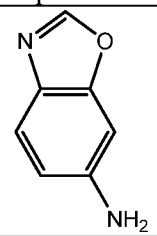
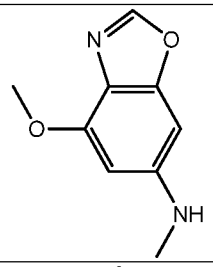
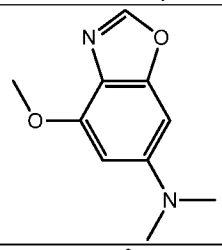
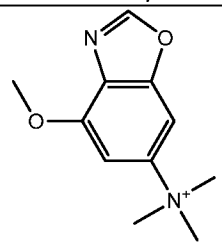
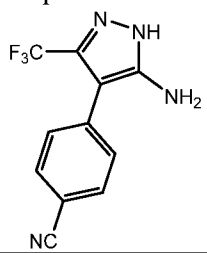
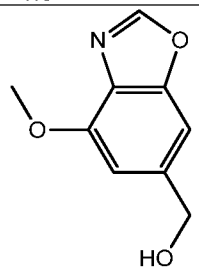
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1100		(500 MHz, DMSO) δ 7.79 (d, J = 8.6 Hz, 1H), 7.59 (d, J = 7.4 Hz, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.31-7.27 (m, 1H), 7.08 (d, J = 8.7 Hz, 1H), 4.10 (s, 3H), 2.42 (s, 3H).	98.0	466.1
C1105		(500 MHz, DMSO) δ 7.59 – 7.56 (m, 1H), 7.54 – 7.50 (m, 4H), 7.48 – 4.42 (m, 1H), 7.05 (d, J = 1.6 Hz, 1H), 4.03 (s, 3H), 2.49 (s, 3H).	95.9	475.0
C1106		(500 MHz, DMSO) δ 7.68 (d, J = 7.3 Hz, 1H), 7.54 – 7.50 (m, 2H), 7.38 – 7.31 (m, 2H), 7.22 (t, J = 7.4 Hz, 1H), 6.77 (d, J = 7.3 Hz, 1H), 3.50 (s, 3H), 2.27 (s, 3H).	95.6	442.0
C1107	Replace **I-1** with 	(500 MHz, DMSO) δ 12.92 (brs, 1H), 7.56 – 7.53 (m, 2H), 7.40 – 7.36 (m, 4H), 6.99 (dd, J = 6.9, 2.1 Hz, 1H), 4.01 (s, 3H).	100	458.9
C1110		(500 MHz, DMSO) δ 8.30 (s, 1H), 7.66 – 7.54 (m, 2H), 7.47 – 7.39 (m, 2H), 7.35 – 7.26 (m, 1H), 7.16 (d, J = 8.1 Hz, 1H), 7.05 (d, J = 6.8 Hz, 1H), 4.04 (s, 3H), 1.96 (s, 3H).	97.9	441.2
C1111		(500 MHz, DMSO) δ 7.86 (d, J = 8.9 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.49 – 7.44 (m, 2H), 7.38 – 7.32 (m, 1H), 7.08 – 7.03 (m, 1H), 4.10 (s, 3H), 2.75 (s, 3H), 2.08 (s, 3H).	100	482.9
C1112		(500 MHz, DMSO) δ 13.15 (brs, 1H), 7.53 – 7.44 (m, 7H), 4.06 (s, 3H), 2.57 (s, 3H).	96.5	466.1

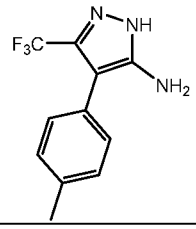
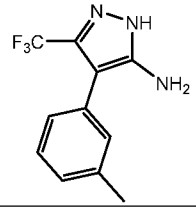
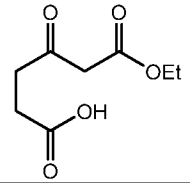
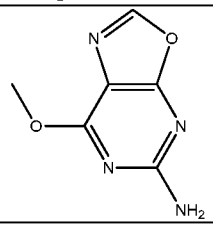
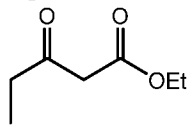
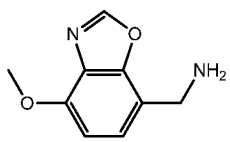
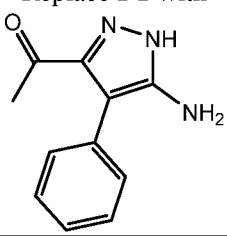
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1113		(400 MHz, DMSO) δ 7.72 (d, J = 8.6 Hz, 1H), 7.57 – 7.54 (m, 2H), 7.41 – 7.35 (m, 2H), 7.27 – 7.22 (m, 1H), 6.95 (d, J = 8.7 Hz, 1H), 4.02 (s, 3H), 2.51 (s, 3H).	97.5	484.2
C1114	Replace **I-1** with 	(500 MHz, DMSO) δ 12.95 (brs, 1H), 7.61 – 7.56 (m, 1H), 7.40 – 7.32 (m, 5H), 6.99 (dd, J = 6.8, 2.2 Hz, 1H), 4.01 (s, 3H), 2.52 (s, 3H).	100	459.8
C1115	Replace **I-1** with 	(500 MHz, DMSO) δ 12.89 (brs, 1H), 7.44 – 7.35 (m, 4H), 7.12 – 7.08 (m, 2H), 6.98 (dd, J = 6.6, 2.5 Hz, 1H), 4.02 (s, 3H), 3.84 (s, 3H), 2.51 (s, 3H)	100	470.9
C1116		(500 MHz, DMSO) δ 11.71 (s, 1H), 7.62 – 7.51 (m, 2H), 7.50 – 7.29 (m, 4H), 6.81 (d,J = 6.9 Hz, 1H), 2.38 (s, 3H).	95.5	428.0
C1117		(500 MHz, DMSO) δ 12.96 (s, 1H), 7.60 (d, J = 7.5 Hz, 2H), 7.48-7.39 (m, 2H), 7.33 – 7.26 (m, 2H), 7.27-7.21 (m, 1H), 7.11 – 7.08 (m, 1H), 6.85 – 6.81 (m, 1H), 5.06 (s, 2H), 2.40 (s, 3H)	99.9	485.1
C1119	Replace **I-1** with 	(500 MHz, DMSO) δ 7.43–7.39 (m, 2H), 7.30–7.27 (m, 2H), 7.15 (tt, J = 9.4, 2.6 Hz), 6.91 (dd, J = 5.8, 3.2 Hz), 4.01 (s, 3H), 2.41 (s, 3H).	100	476.9
C1120	Replace **I-1** with 	(500 MHz, DMSO) δ 12.94 (brs, 1H), 7.44 (t, J = 7.9 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.07 (dd, J = 17.0, 9.2 Hz, 3H), 7.00 – 6.95 (m, 1H). 4.01 (s, 3H), 3.82 (s, 3H)	100	470.9

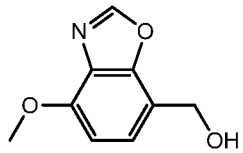
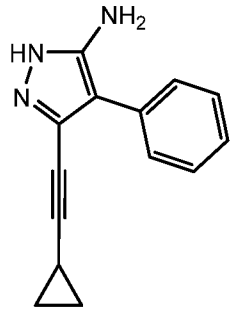
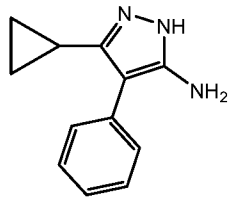
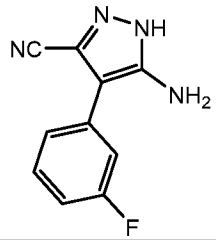
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1122		(500MHz, CD3CN) δ 12.52 (s, 1H), 8.31 (s, 1H), 7.84 (s, 1H), 7.36 (d, J = 7.4Hz, 2H), 7.26 – 7.20 (m, 2H), 7.17 – 7.12 (m, 1H), 6.86 (d, J = 9.3Hz, 1H), 3.82 (s, 3H), 2.54 (s, 3H)	98.6	484.1
C1123		(500 MHz, DMSO) δ 7.56 – 7.47 (m, 4H), 7.44 (d, J = 6.7 Hz, 1H), 6.40 (d, J = 1.5 Hz, 1H), 6.23 (d, J = 1.6 Hz, 1H). 5.37 (brs, 1H), 3.90 (s, 3H), 2.40 (s, 3H)	100	456.0
C1125		(500 MHz, DMSO) δ 7.68 (d, J = 8.7 Hz, 2H), 7.60 (d, J = 7.6 Hz, 4H), 7.43 (t, J = 7.7 Hz, 4H), 7.30 (t, J = 7.4 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 4.10 (s, 5H), 3.43 (s, 6H), 2.49 (s, 6H).	97.8	519.0
C1126		(400 MHz, DMSO) δ 7.70 – 7.64 (m, 1H), 7.58 – 7.54 (m, 2H), 7.52 – 7.43 (m, 3H), 7.39 – 7.29 (m, 1H), 4.51 (s, 3H), 2.52 (s, 3H).	95	466.0
C1127	Replace **I-1** with 	(500 MHz, DMSO) δ 8.73 (d, J = 4.2 Hz, 1H), 7.97 (t, J = 7.7 Hz, 1H), 7.90 – 7.85 (m, 1H), 7.46 – 7.31 (m, 3H), 6.98 (dt, J = 7.9, 4.5 Hz, 1H),4.02 (s, 3H), 2.59 (s, 3H).	98.4	442.0
C1128 also C1135 (HCl salt)		(500 MHz, DMSO) δ 8.15 (s, 2H), 7.60 (d, J = 7.4 Hz, 2H), 7.47 – 7.40 (m, 3H), 7.35 – 7.24 (m, 1H), 7.05 (d, J = 1.2 Hz, 1H), 4.17 (s, 2H), 4.04 (s, 3H), 2.39 (s, 3H).	98.9	469.9
C1129	Replace **I-1** with 	(500 MHz, DMSO) δ 8.79 (brs, 1H), 8.60 (brs, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.54 (s, 1H), 7.33 (d, J = 5.3 Hz, 2H), 6.97 – 6.92 (m, 1H), 4.02 (s, 3H), 2.44 (s, 3H).	98.3	441.9

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1130		(500 MHz, MeOD) δ 8.00 (d, J = 8.7 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.49 – 7.45 (m, 2H), 7.43 – 7.38 (m, 1H), 7.03 (d, J = 8.7 Hz, 1H), 4.13 (s, 3H), 2.48 (s, 3H).	99.1	485.0
C1133	Replace **I-1** with 	(500 MHz, DMSO) δ 13.12 (brs, 1H). 7.71 – 7.59 (m, 1H), 7.42 – 7.35 (m, 2H), 7.35 – 7.28 (m, 2H), 6.98 (dd, J = 6.5, 2.5 Hz, 1H). 4.01 (s, 3H), 2.53 (s, 3H)	99.3	477.0
C1134	Replace **I-10** with 	(500 MHz, DMSO) δ 7.60 (d, J = 6.9 Hz, 2H), 7.44 (t, J = 7.3 Hz, 2H), 7.33-7.28 (m , 3H), 6.93 – 6.87 (m, 1H), 4.69 (m, 1H), 4.56 (m, 1H), 4.48 (m, 1H), 3.99 (s, 3H), 3.53 (t, J = 7.3 Hz, 1H), 3.24 (m, 1H), 1.37 – 1.12 (m, 5H), 1.07 – 0.99 (m, 1H).	97.0	541.2
C1137	Replace **I-10** with 	(500 MHz, DMSO) δ 7.61 (d, J = 7.6 Hz, 2H), 7.44 (dd, J = 10.6, 4.9 Hz, 2H), 7.34 – 7.25 (m, 3H), 6.91 (dd, J = 7.6, 1.4 Hz, 1H), 4.43 (q, J = 12.6 Hz, 2H), 4.01 (s, 3H), 2.60 (s, 3H).	97.4	503.0
C1138	Replace **I-10** with 	(500 MHz, DMSO) δ 7.60 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.34 – 7.25 (m, 3H), 6.91 (dd, J = 7.5, 1.6 Hz, 1H), 4.95 (s, 2H), 4.01 (s, 3H), 3.07 (s, 3H).	99.2	519.1
C1140	Replace **I-10** with 	(500 MHz, DMSO) δ 10.67 (s, 1H), 10.10 (s, 1H), 8.02 (s, 1H), 7.58 – 7.51 (m, 4H), 7.47 (t, J = 6.9 Hz, 1H), 7.28 (t, J = 8.4 Hz, 1H), 6.66-6.65 (m, 2H), 4.27 (q, J = 7.1 Hz, 2H), 3.70 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H).	97.3	513.1
C1141		(500 MHz, DMSO) δ 8.40 (brs, 2 H), 7.85 (d, J = 1.4 Hz, 1H), 7.60 (d, J = 7.3 Hz, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.36 (d, J = 1.4 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 4.10 (s, 3H), 2.49 (s, 2H).	99.4	482.9

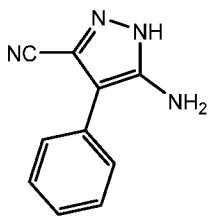
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1144	Replace **I-10** with 	500 MHz, DMSO) δ 9.48 (s, 1H), 7.62 (d, J = 7.7 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 7.18 (t, J = 8.3 Hz, 1H), 6.57 (dd, J = 8.2, 2.9 Hz, 2H), 3.66 (s, 3H), 2.54 (s, 3H).	98.8	469.1
C1147	Replace **I-10** with 	(500 MHz, DMSO) δ 9.98 (s, 1H), 7.82 (s, 1H), 7.56 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 7.6 Hz, 2H), 7.38 (s, 1H), 7.25 (t, J = 8.4 Hz, 1H), 6.64 (d, J = 8.3 Hz, 2H), 3.69 (s, 3H).	98.4	485.1
C1148	Replace **I-1** with 	(500 MHz, DMSO) δ 8.05 – 8.00 (m, 1H), 7.85 – 7.80 (m, 1H), 7.74 – 7.70 (m, 1H), 7.70 – 7.62 (m, 1H), 7.40 – 7.33 (m, 2H), 6.97 – 6.93 (m, 1H), 4.02 (s, 3H), 2.45 (s, 3H).	99.2	466.0
C1149		(500 MHz, DMSO) δ8.09 (s, 1H), 7.89 (s, 1H), 7.54 – 7.51 (m, 4H), 7.51 – 7.48 (m, 2H), 7.47– 7.43 (m, 1H), 4.05 (s, 3H), 2.52 (s, 3H).	100	484.2
C1150		(500 MHz, DMSO) δ 13.04 – 12.93 (m, 1H), 8.20 (s, 1H), 7.51 (d, J = 7.6 Hz, 2H), 7.39 – 7.34 (m, 2H), 7.24 (t, J = 7.4 Hz, 1H), 4.04 (s, 3H), 2.60 (s, 3H), 2.52 (s, 3H).	97.4	500.0
C1154		(500 MHz, DMSO) δ 7.61 (d, J = 7.4 Hz, 2H), 7.45 – 7.39 (m, 2H), 7.31 – 7.25 (m, 1H), 6.63 (d, J = 8.4 Hz, 1H), 6.52 (d, J = 8.4 Hz, 1H), 4.90 (s, 2H), 3.88 (s, 3H), 2.27 (s, 3H).	98.2	456.0
C1155		(500 MHz, DMSO) δ 13.15 (brs, 1H), 7.88 (s, 1H), 7.55 (d, J = 7.4 Hz, 2H), 7.52 – 7.46 (m, 3H), 7.41 (d, J = 7.1 Hz, 1H). 4.06 (s, 3H).	100	484.9

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1156		(500 MHz, DMSO) δ 7.54 (d, J = 7.2 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 6.81 (s, 1H), 6.64 (d, J = 8.3 Hz, 1H), 2.39 (s, 3H).	94.6	424.1
C1161		(500 MHz, DMSO) δ 7.56 (d, J = 7.7 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.34 (s, 1H), 6.33 (d, J = 1.7 Hz, 1H), 6.18 (d, J = 1.7 Hz, 1H), 5.87 (s, 1H), 3.91 (s, 3H), 2.72 (s, 3H), 2.32 (s, 3H)	100	470.0
C1162		(500 MHz, DMSO) δ 7.55 (d, J = 7.3 Hz, 2H), 7.48 (t, J = 7.4 Hz, 2H), 7.39 (s, 1H), 6.59 (s, 1H), 6.33 (s, 1H), 4.00 (s, 3H), 2.98 (s, 6H), 2.38 (s, 3H)	99.7	484.0
C1163	 (formate salt)	(500 MHz, DMSO) δ 8.45 (s, 1H), 8.06 (d, J = 2.4 Hz, 1H), 7.60 (d, J = 7.4 Hz, 2H), 7.47 (d, J = 2.4 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.35 – 7.25 (m, 1H), 4.15 (s, 3H), 3.69 (s, 9H), 2.45 (s, 3H)	98.9	498.0
C1164	Replace **I-1** with 	(500 MHz, DMSO) δ 7.90 (s, 4H), 7.30 (s, 1H). 7.29 (d, J = 2.0 Hz, 1H), 6.92 (dd, J = 5.4, 3.6 Hz, 1H). 4.01 (s, 3H), 2.40 (s, 3H)	98.5	465.9
C1166		(500 MHz, DMSO) δ 7.56 (d, J = 7.6 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.39 (s, 1H), 7.25 (s, 1H), 6.91 (s, 1H), 5.34 (s, 1H), 4.63 (s, 2H), 4.00 (s, 3H), 2.42 (s, 3H).	399.2	99.7

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1171	Replace **I-1** with 	(500 MHz, DMSO) δ 12.91 (s, 1H), 7.40–7.37 (m, 4H), 7.37–7.33 (m, 2H), 6.98 (dd, J = 6.9, 2.2 Hz, 1H), 4.01 (s, 3H), 2.50 (s, 3H), 2.40 (s, 3H)	100	455.1
C1172	Replace **I-1** with 	(500 MHz, DMSO) δ 12.93 (s, 1H), 7.45–7.41 (m, 1H), 7.39–7.36 (m, 2H), 7.31 (d, J = 7.2 Hz, 2H), 7.27 (d, J = 7.7 Hz, 1H). 4.01 (s, 3H), 2.52 (s, 3H), 2.40 (s, 3H).	100	455.1
C1173	Replace **I-10** with 	(500 MHz, DMSO) δ 12.02 (s, 1H), 7.66 (m, 2H), 7.46 – 7.39 (m, 2H), 7.29 (m, 3H), 6.93 – 6.89 (m, 1H), 4.01 (s, 3H), 2.96 (t, J = 6.5 Hz, 2H), 2.60 (t, J = 7.3 Hz, 2H).	98.6	499.3
C1174		(500 MHz, DMSO) δ 7.66 – 7.56 (m, J = 7.6 Hz, 2H), 7.46 – 7.38 (m, J = 7.4 Hz, 2H), 7.31 – 7.24 (m, 1H), 6.80 (s, 2H), 4.01 (s, 3H), 2.30 (s, 3H)	95.7	457.9
C1183	Replace **I-10** with 	(500 MHz, DMSO) δ 7.66 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.30 – 7.25 (m, 3H), 6.90 (dd, J = 5.6, 3.4 Hz, 1H), 4.00 (s, 3H), 2.66 (q, J = 7.5 Hz, 2H), 1.07 (t, J = 7.5 Hz, 3H).	96.8	455.0
C1191		(500 MHz, DMSO) δ 13.00 (s, 1H), 8.36 (s, 3H), 7.60 – 7.38 (m, 6H), 7.04 (d, J = 8.6 Hz, 1H), 4.26 (d, J = 5.5 Hz, 2H), 4.03 (s, 3H), 2.47 (s, 3H).	98.6	470.1
C1210	Replace **I-1** with 	(500MHz, DMSO-d_6): δ ppm = 7.60 (d, J = 7.5Hz, 2H), 7.33 (t, J = 7.5Hz, 2H), 7.27-7.24 (m, 2H), 7.20 (t, J = 7.5Hz, 1H), 7.10 (br s, 1H), 6.89 (dd, J = 6.0Hz, 3.0Hz, 1H), 4.00 (s, 3H), 2.63 (s, 3H), 2.35 (s, 3H).	99.9	414.41

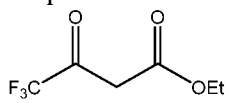
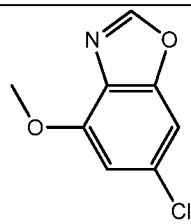
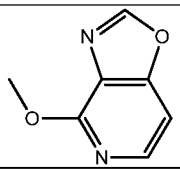
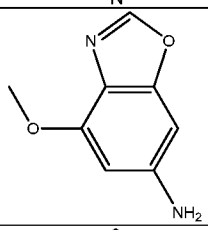
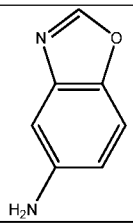
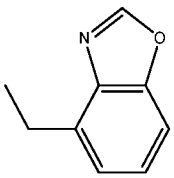
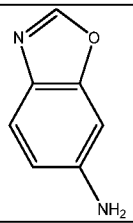
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1224		(500 MHz, DMSO): δ 8.35 (s, 1H), 7.62 (d, *J* = 7.4 Hz, 2H), 7.45 – 7.41 (m 2H), 7.34 – 7.20 (m, 2H), 6.88 (d, *J* = 8.4 Hz, 1H). 4.71 (s, 2H), 3.99 (s, 3H), 2.33 (s, 3H).	96.0	471.1
C1228	Replace **I-1** with 	(500MHz, DMSO-d_6): δ ppm = 8.05 (br s, 1H), 7.41 (t, *J* = 8.0Hz, 2H), 7.27 (d, *J* = 4.5Hz, 2H), 7.24-7.15 (m, 2H), 7.08 (br s, 1H), 6.99 (br s, 1H), 6.90 (t, *J* = 4.5Hz, 1H), 4.00 (s, 3H), 2.43 (s, 3H), 1.63-1.58 (m, 1H), 0.95-0.91 (m, 2H), 0.80-0.77 (m, 2H).	99.9	436.46
C1242	Replace **I-1** with 	(500MHz, DMSO-d_6): δ ppm = 7.63 (m, 2H), 7.51 (t, *J* = 7.5Hz, 2H), 7.39-7.36 (m, 1H), 7.34-7.31 (m, 2H), 6.95 (dd, *J* = 7.0Hz, 2.0 Hz, 1H), 4.00 (s, 3H), 2.45 (s, 3H), 1.97-1.89 (m, 1H), 1.00-0.93 (m, 4H)	98.2	412.44
C1283	Replace **I-1** with 	(500MHz, DMSO) δ ppm = 8.03 (ddd, *J* = 11.0 Hz, 2.5 Hz, 1.5 Hz, 1H), 7.94-7.92 (m, 1H), 7.54-7.50 (m, 1H), 7.28 (dd, *J* = 4.5Hz, 0.5 Hz, 2H), 7.13-7.09 (m, 1H), 6.91 (quint, *J* = 4.5 Hz, 1H), 4.00 (s, 3H), 2.45 (s, 3H).	99.9	416.1

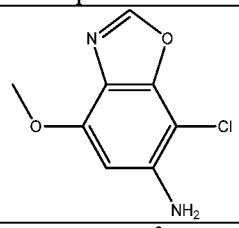
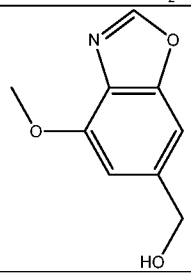
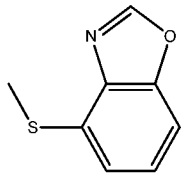
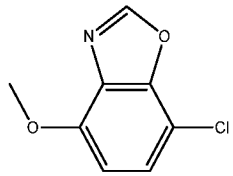
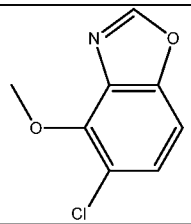
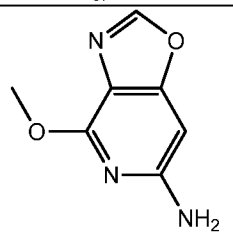
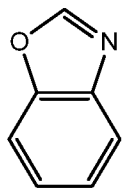
[00429] The compounds in Table 5A below were synthesized similarly to the methods described in Steps 1-2 above, optionally substituting the listed compound as indicated for **I-15**, and/or substituting for **I-10** where indicated and substituting **I-1** with

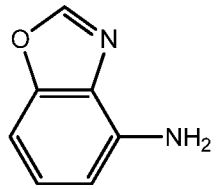
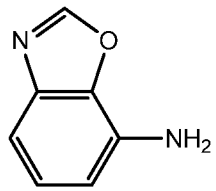
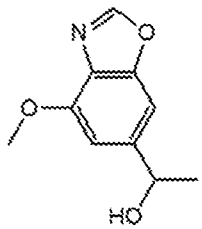
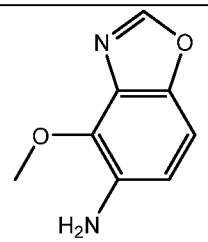
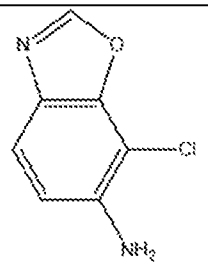
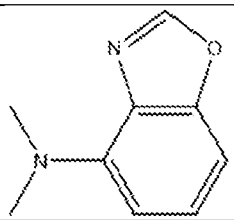
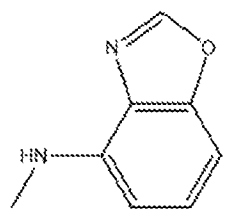


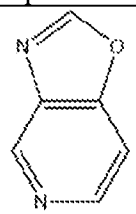
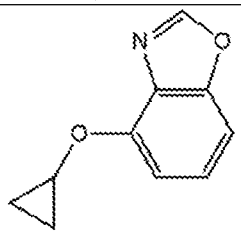
to provide the suitable analog of **I-11** (per Example 3).

Table 5A

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1118	Replace **I-10** with 	(500 MHz, DMSO) δ 8.05 – 8.00 (m, 2H), 7.56 – 7.50 (m, 2H), 7.39 – 7.29 (m, 3H), 6.95 (dd, J = 7.9, 0.8 Hz, 1H), 4.00 (s, 3H).	99.5	452.2
C1160		(500 MHz, DMSO) δ 8.01 (d, J = 7.0 Hz, 2H), 7.52 – 7.45 (m, 3H), 7.31 (t, J = 7.4 Hz, 1H), 6.99 (d, J = 1.7 Hz, 1H), 4.01 (s, 3H), 2.46 (s, 3H).	98.2	431.9
C1167		(500 MHz, DMSO) δ 8.12 – 8.01 (m, 3H), 7.54 – 7.42 (m, 3H), 7.31 (t, J = 7.3 Hz, 1H), 2.49 (s, 3H).	399.2	99.7
C1175		(500MHz, DMSO) δ 8.08 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.8 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 6.38 (d, J = 1.5 Hz, 1H), 6.20 (d, J = 1.5 Hz, 1H), 3.91 (s, 3H), 2.35 (s, 3H).	95.3	413.0
C1181		(500MHz, DMSO) δ 8.38 (s, 2H), 8.07 (d, J = 7.3 Hz, 2H), 7.48 (t, J = 7.8 Hz, 2H), 7.35 – 7.19 (m, 2H), 6.85 (d, J = 1.8 Hz, 1H), 6.61 (dd, J = 8.6, 2.1 Hz, 1H). 2.40 (s, 3H).	97.2	382.9
C1188		(500MHz, DMSO) δ 13.16 (brs, 1H), 7.71 (d, J = 6.3 Hz, 2H), 7.62–7.57 (m, 3H), 7.49 (t, J = 7.3 Hz, 1H), 7.36 (t, J = 7.8 Hz, 1H), 7.26 (d, J = 7.5 Hz, 1H). 2.99 (q, J = 7.5 Hz, 2H), 2.57 (s, 3H), 1.34 (t, J = 7.6 Hz, 3H).	100	396.1
C1193		(500 MHz, DMSO) 8.16 – 7.99 (m, 2H), 7.59 – 7.42 (m, 2H), 7.35 (d, J = 8.4 Hz, 1H), 7.34 – 7.23 (m, 1H), 6.78 (d, J = 1.7 Hz, 1H), 6.60 (dd, J = 8.4, 2.1 Hz, 1H), 5.23 (s, 2H), 2.35 (s, 3H).	100	383.1

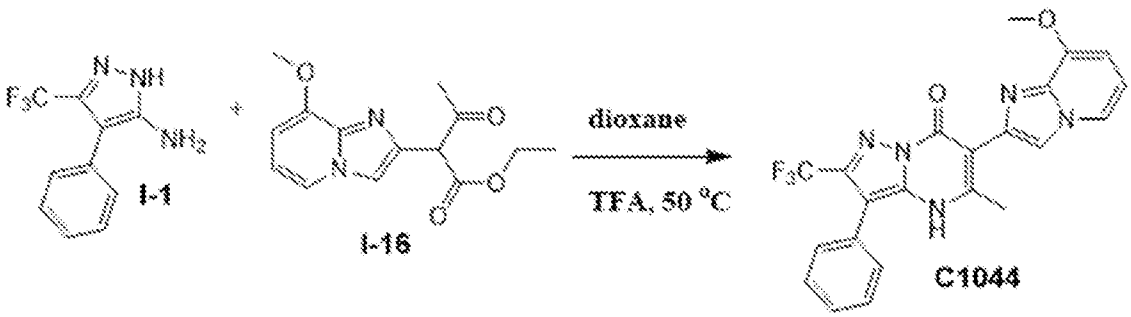
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1202		(400 MHz, DMSO): δ 13.10 (brs, 1H): δ 7.68 (d, J = 7.3 Hz, 2H), 7.59 (t, J = 7.6 Hz, 2H), 7.50 (t, J = 7.2 Hz, 1H), 6.47 (s, 1H), 5.67 (s, 2H), 3.92 (s, 3H), 2.48 (s, 3H).	96.9	447.2
C1203		(500 MHz, DMSO): δ 7.75 (m, 2H), 7.58 (t, J = 7.6 Hz, 2H), 7.49–7.45 (m, 1H), 7.29 (s, 1H), 6.94 (s, 1H), 4.64 (s, 2H), 4.01 (s, 3H).	94.9	428.0
C1204		(500MHz, DMSO-d6): δ ppm = 8.36 (br s, 1H), 8.08-8.05 (m, 2H), 7.49-7.46 (m, 3H), 7.32 (d, J = 7.5Hz, 1H), 7.31-7.28 (m, 1H), 7.18 (dd, J = 7.5Hz, 0.5Hz, 1H), 2.63 (s, 3H), 2.47 (s, 3H).	97.0	413.46
C1205		(500MHz, DMSO-d6): δ ppm = 8.34 (br s, 1H), 8.07-8.04 (m, 2H), 7.48 (t, J = 8.0Hz, 2H), 7.36 (d, J = 9.0Hz, 1H), 7.32-7.28 (m, 1H), 6.94 (d, J = 9.0Hz, 1H), 4.00 (s, 3H), 2.45 (s, 3H).	95.7	431.84
C1206		(500MHz, DMSO-d6): δ ppm = 8.13 (s, 1H), 8.02 (d, J = 7.5Hz, 2H), 7.51-7.48 (m, 2H), 7.39-7.35 (m, 2H), 7.32 (t, J = 7.5Hz, 1H), 4.38 (s, 3H), 2.53 (s, 3H).	96.8	431.84
C1218		(500 MHz, DMSO) δ 8.10 – 8.02 (m, J = 8.3, 1.1 Hz, 2H), 7.51 – 7.42 (m, J = 7.8 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 6.22 (s, 1H), 5.89 (s, 2H), 3.95 (s, 3H), 2.34 (s, 3H).	98	414.1
C1222		(500 MHz, DMSO): δ 8.11 – 8.04 (m, 2H), 7.77 – 7.72 (m, 1H), 7.72 – 7.69 (m, 1H), 7.52 – 7.45 (m, 2H), 7.39 – 7.33 (m, 2H), 7.33 – 7.27 (m, 1H), 7.08 (s, 1H), 2.47 (s, 3H).	97.0	368.0

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1223		(500 MHz, DMSO): δ 7.85 – 7.78 (m, 2H), 7.56 (t, J = 7.7 Hz, 2H), 7.48 – 7.42 (m, 1H), 7.08 (t, J = 8.0 Hz, 1H), 6.85 (d, J = 7.9 Hz, 1H), 6.56 (d, J = 7.9 Hz, 1H), 5.66 (brs, 1H), 2.49 (s, 3H).	94.0	383.1
C1230		(400 MHz, DMSO): δ 8.07 (d, J = 7.5 Hz, 2H), 7.49 (t, J = 7.8 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 7.07 – 7.00 (m, 1H), 6.96 – 6.90 (m, 1H), 6.61 (d, J = 7.8 Hz, 1H), 5.43 (s, 2H), 2.37 (s, 3H).	95.6	383.1
C1240		(500 MHz, DMSO): δ 8.09 – 8.07 (m, 2H), 7.50 – 7.47 (m, 2H), 7.31 – 7.28 (m, 1H), 7.23 (s, 1H), 6.91 (s, 1H), 5.28 (d, J = 4.3 Hz, 1H), 4.87 – 4.81 (m, 1H), 4.01 (s, 3H), 2.42 (s, 3H), 1.40 (d, J = 6.4 Hz, 3H).	97.6	442.1
C1250		(400 MHz, DMSO): δ 8.08 (d, *J* = 7.3 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 4.66 (s, 2H), 4.20 (s, 3H), 2.46 (s, 3H).	97.1	413.1
C1271		(500 MHz, DMSO) δ 8.08 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 5.53 (s, 2H), 2.37 (s, 3H).	100	417.2
C1272		(400 MHz, DMSO) δ 7.73 (d, *J* = 6.3 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.24 (t, *J* = 8.1 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 3.21 (s, 6H), 2.55 (s. 3H).	94.5	411.2
C1274		(500 MHz, DMSO) δ 8.01 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.40 (d, *J* = 7.9 Hz, 1H), 6.00 (s, 1H), 2.88 (s, 3H), 2.42 (s, 3H).	100	397.2

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1275		(500 MHz, MeOD) δ 8.87 (s, 1H), 8.42 – 8.37 (m, 1H), 8.35 (s, 2H), 7.86 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.66 (s, 1H), 7.41 – 7.36 (m, 1H), 7.27 – 7.23 (m, 1H), 2.55 (s, 3H).	94.1	369.2
C1277		(500 MHz, DMSO) δ 8.07 (dd, J = 8.4, 1.2 Hz, 2H), 7.47 (dd, J = 11.1, 4.6 Hz, 2H), 7.32 – 7.26 (m, 3H), 7.15 (dd, J = 6.1, 2.9 Hz, 1H), 4.15-4.11 (m, 1H), 2.42 (s, 3H), 0.86 – 0.77 (m, 4H).	97.2	424.2

Example 5

[00430] Synthesis of 6-(8-methoxyimidazo[1,2-*a*]pyridin-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1044**) was carried out in one step as follows:

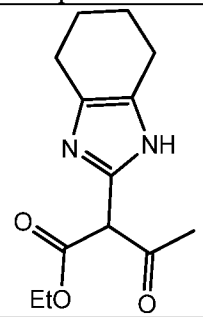
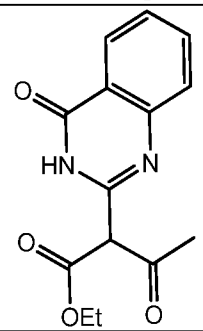
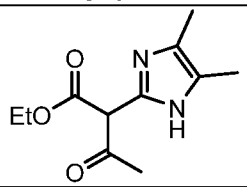
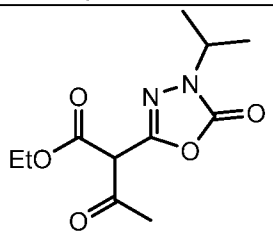
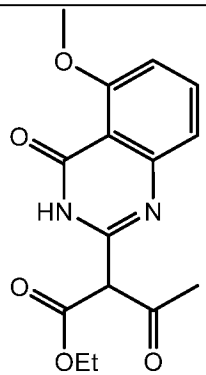


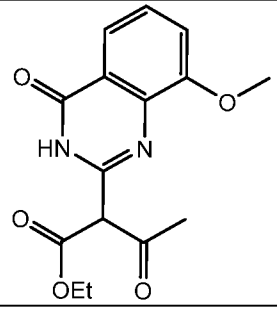
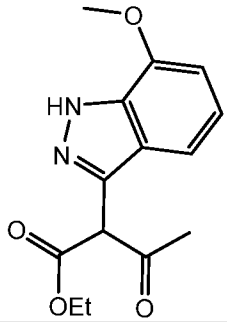
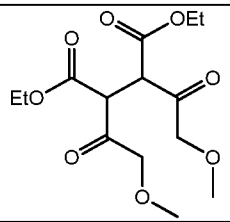
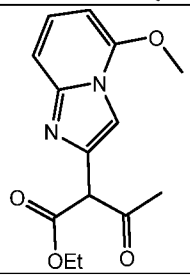
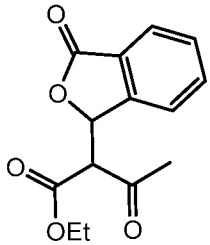
[00431] **Step 1**: To a solution of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine (**I-1**, 55.0 mg, 242 µmol) and ethyl 2-(8-methoxyimidazo[1,2-*a*]pyridin-2-yl)-3-oxobutanoate (**I-16**, 73.6 mg, 266 µmol) in dioxane (807 µL) was added TFA (403 µL) and the reaction mixture was heated at 50 °C for 6h. LCMS shows reaction was completed. The volatiles were removed *in vacuo*. The crude material was purified by Reverse Phase chromatography on a Companion Combiflash using 10g C18 column with a gradient elution of 20-50% MeCN/H_2O (0.1% ammonium formate buffer) over 15 min and a flow rate of 30 mL/min. The clean fractions were combined and lyophilized to afford the compound **C1044**. ^{1}HNMR (500 MHz, DMSO) δ 12.46 (s, 1H), 8.31 (s, 1H), 8.26 (d, *J* = 6.6 Hz, 1H), 7.55 – 7.48 (m, 4H), 7.46 (s, 1H), 6.85 (s, 1H), 6.70 (s, 1H), 3.97 (s, 3H), 2.71 – 2.60 (m, 3H). MS (m/z): 440.2 $[M+1]^+$, 98.1%.

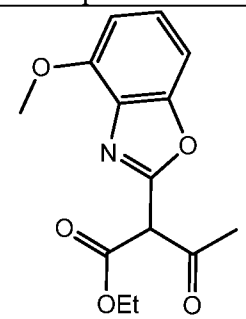
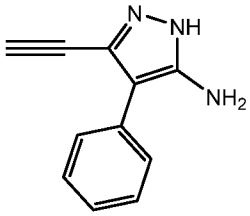
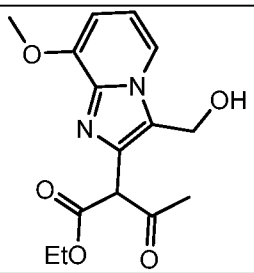
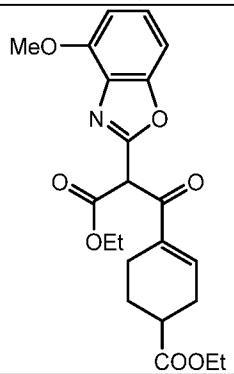
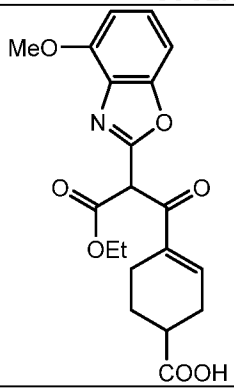
[00432] Table 6 below provides additional compounds that can be synthesized similarly to the methods described in the above step, substituting the listed compound as indicated for **I-16**,

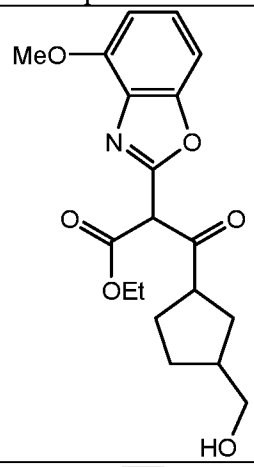
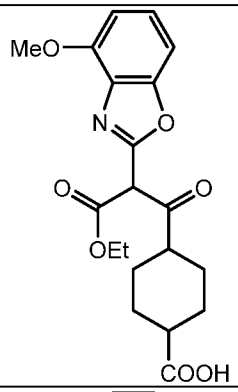
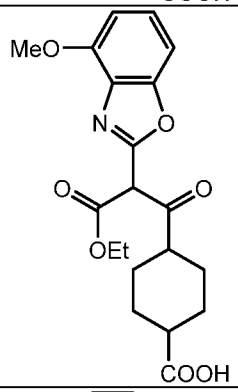
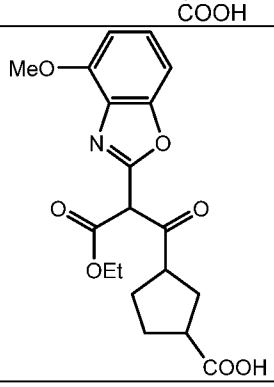
as well as substituting for **I-1** where indicated. Data for compounds synthesized is provided in columns 3-5.

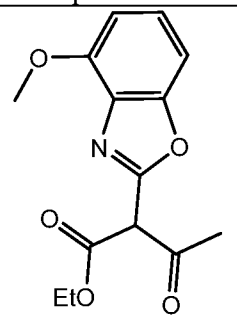
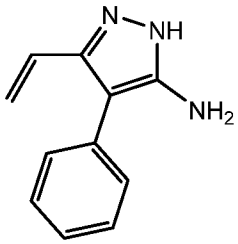
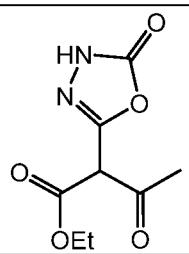
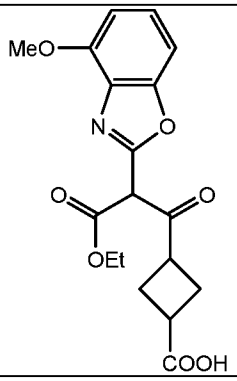
Table 6

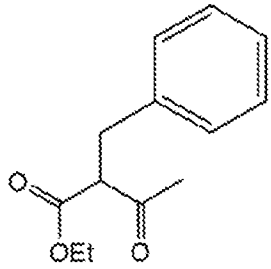
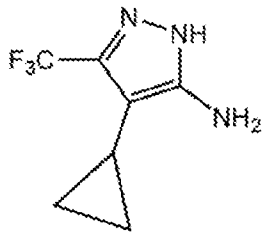
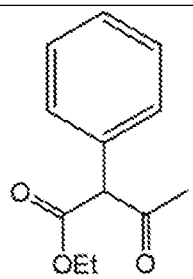
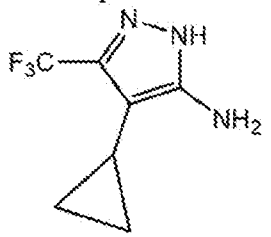
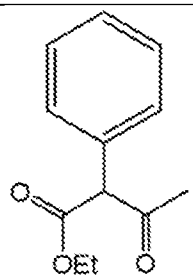
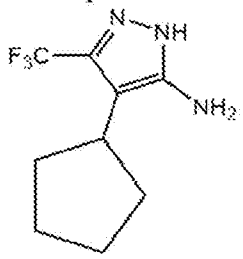
Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1017		(500 MHz, DMSO) δ 7.58 (d, J = 7.6 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 2.64 – 2.57 (m, 4H), 2.39 (s, 3H), 1.84 – 1.78 (m, 4H).	98.6	414.2
C1019		(500 MHz, DMSO) δ 12.76 (s, 1H), 12.45 (s, 1H), 8.18 (dd, J = 8.0, 1.3 Hz, 1H), 7.91 – 7.78 (m, 1H), 7.70 (d, J = 7.9 Hz, 1H), 7.60 – 7.42 (m, 6H), 2.44 (s, 3H).	99.1	438.2
C1021		(500 MHz, MeOD) δ 7.63 (s, 2H), 6.71 (d, J = 7.5 Hz, 2H), 6.62 (t, J = 7.6 Hz, 2H), 6.54 (t, J = 7.4 Hz, 1H), 1.53 (s, 3H), 1.50 (s, 6H).	99.0	388.1
C1023		(500 MHz, DMSO) δ 7.52-7.51 (m, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 4.32 – 4.24 (m, 1H), 2.34 (s, 3H), 1.34 (d, J = 6.7 Hz, 6H).	98.9	420.2
C1024		(500 MHz, DMSO) δ 12.66 (s, 1H), 7.61 (t,J = 8.2 Hz, 1H), 7.48 – 7.40 (m, 4H), 7.38 – 7.28 (m, 1H), 7.10 (s, 1H), 6.96 – 6.91 (m, 1H), 3.81 (s, 3H), 2.48 – 2.44 (m, 3H).	98.9	468.1

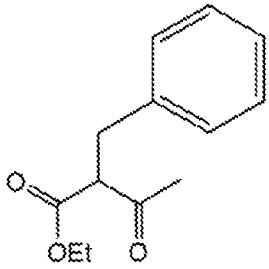
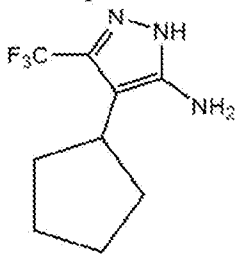
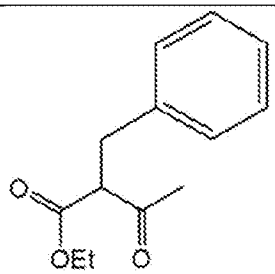
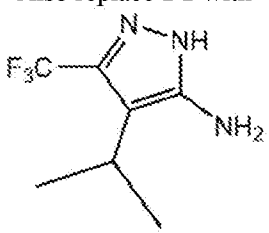
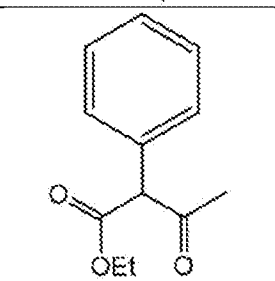
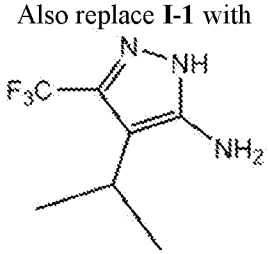
Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1025		(500 MHz, DMSO) δ 12.74 (s, 1H), 12.41 (s, 1H), 7.73 (dd, J = 8.0, 1.3 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.53 – 7.46 (m, 4H), 7.41 (dd, J = 8.2, 1.2 Hz, 1H), 3.91 (s, 3H), 2.40 (s, 3H).	99.1	468.2
C1026		(500 MHz, DMSO) δ 13.43 (s, 1H), 12.52 (s, 1H), 7.58 – 7.46 (m, 5H), 7.10 (d, J = 8.1 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 6.86 (d, J = 7.4 Hz, 1H), 3.99 (s, 3H), 2.22 (s, 3H).	98.7	440.1
C1029		(500 MHz, DMSO) δ 12.62 (s, 2H), 7.56 – 7.47 (m, 10H), 4.28 (d, J = 1.4 Hz, 4H), 3.20 (s, 6H).	99.1	645.2
C1057		(500 MHz, DMSO) δ 12.45 (br s, 1H), 8.05 (s, 1H), 7.51 – 7.13 (m, 7H), 6.46 (s, 1H), 4.10 (s, 3H), 2.56 (s, 3H).	97.7	440.2
C1168		(500 MHz, DMSO) δ 12.53 (s, 1H), 7.90 (d,J = 7.6 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.61 (t,J = 7.5 Hz, 1H), 7.56 – 7.46 (m, 3H), 7.44 (d,J = 6.7 Hz, 2H), 6.88 (s, 1H), 3.57 (s, 3H).	426.0	97.4

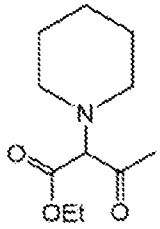
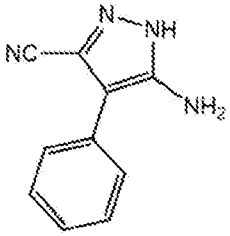
Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1211	 Also replace **I-1** with 	(500MHz, DMSO-d_6): δ ppm = 8.30 (br s, 1H), 8.22-8.20 (m, 2H), 7.39 (t, J = 8.0Hz, 2H), 7.27-7.23 (m, 2H), 7.19-7.16 (m, 1H), 6.88 (dd, J = 5.5Hz, 3.0Hz, 1H), 4.38 (s, 1H), 4.00 (s, 3H), 2.42 (s, 3H)	97.1	396.41
C1215		(500 MHz, DMSO) δ 12.54 (s, 1H), 8.23 – 7.98 (m, 1H), 7.62 – 7.47 (m, 4H), 7.46 – 7.33 (m, 1H), 7.04 – 6.84 (m, 1H), 6.83 – 6.61 (m, 1H), 5.23 – 4.98 (m, 1H), 4.65 (d, J = 4.8 Hz, 2H), 3.96 (s, 3H), 2.25 (s, 3H).	98.06	470.0
C1233		(500 MHz, DMSO) δ 7.62 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.31 – 7.22 (m, 3H), 6.88 (dd, J = 6.9, 2.2 Hz, 1H), 5.51 (s, 1H), 4.04 – 3.94 (m, 5H), 2.37 – 2.34 (m, 1H), 2.06 – 1.88 (m, 2H), 1.55-1.47 (m, 1H), 1.26 (t, J = 6.9 Hz, 3H), 1.17 – 1.05 (m, 3H).	96.6	579.2
C1234		(500 MHz, DMSO) δ 12.99 (s, 1H), 12.15 (s, 1H), 7.53-7.48 (m, 4H), 7.33-7.30 (m, 3H), 6.99 – 6.91 (m, 1H), 5.89 (s, 1H), 4.00 (s, 3H), 2.30 – 1.85 (m, 4H), 1.45-1.40 (m, 1H), 1.25-1.22 (m, 2H).	96.2	551.2

Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1236		(500 MHz, DMSO) δ 7.74-7.72 (m, 2H), 7.44 – 7.39 (m, 2H), 7.30 – 7.23 (m, 3H), 6.92-6.90 (m, 1H), 4.36-4.32 (m, 1H), 4.02-4.01 (m, 3H), 3.26 – 3.16 (m, 2H), 1.96 – 1.84 (m, 3H), 1.71 – 1.66 (m, 1H), 1.57 – 1.51 (m, 2H), 1.47-1.41 (m, 1H).	98.3	525.3
C1237		(500 MHz, DMSO) δ 12.27 (s, 1H), 12.03 (s, 1H), 7.74 – 7.29 (m, 7H), 6.94 (s, 1H), 4.03 (s, 3H), 2.78-2.72 (m, 1H), 2.14 – 2.03 (m, 1H), 1.94 – 1.80 (m, 4H), 1.73-1.68 (m, 2H), 1.23-1.16 (m,2H). (Isomer 1)	99.6	553.2
C1238		(500 MHz, DMSO) δ 12.73 (s, 1H), 11.99 (s, 1H), 7.74-7.69 (m, 2H), 7.53-7.41 (m,5H), 6.92-6.88 (m, 1H), 4.03 (s, 3H), 2.87 – 2.79 (m, 1H), 2.47 – 2.41 (m, 1H), 2.12 – 2.04 (m, 2H), 1.73-1.70 (m, 2H), 1.67 – 1.55 (m, 2H), 1.40 – 1.29 (m, 2H). (Isomer 2)	98.7	553.2
C1239		(500 MHz, DMSO) δ 7.73 (d, J = 7.4 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.34 – 7.21 (m, 3H), 6.91 (dd, J = 5.0, 4.0 Hz, 1H), 4.01 (s, 3H), 2.67 – 2.60 (m, 1H), 2.53 – 2.51 (m, 1H), 2.09-2.04 (m, 2H), 1.98 – 1.85 (m, 2H), 1.79 – 1.67 (m, 2H).	99.5	539.2

Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1241	 Also replace **I-1** with 	(500MHz, DMSO-d_6): δ ppm = 8.87 (br s, 0.5H), 8.34 (br s, 0.5H), 7.58 (d, J = 7.5Hz, 2H), 7.41 (t, J = 7.5Hz, 2H), 7.27-7.22 (m, 3H), 7.12 (br s, 1H), 6.88 (dd, J = 6.0Hz, 2.5Hz, 1H), 6.81 (dd, J = 17.5Hz, 11.0Hz, 1H), 6.00 (dd, J = 17.5Hz, 2.0Hz, 1H), 5.34 (dd, J = 11.0Hz, 2.0Hz, 1H), 4.00 (s, 3H), 2.37 (s, 3H)	97.5	398.42
C1247		(500MHz, DMSO)δ 12.94 (bs, 1H), 12.49 (s, 1H), 7.52 – 7.40 (m, 5H), 2.39 (s, 3H).	97.1	378.1
C1252		(500 MHz, DMSO) δ 7.74 (d, J = 7.7 Hz, 2H), 7.44-7.41 (m, 2H), 7.32 – 7.24 (m, 3H), 6.92-6.89 (m, 1H), 4.03-4.01 (m, 3H), 3.83-3.66 (m, 1H), 2.97 – 2.83 (m, 1H), 2.42-2.36 (m, 2H), 2.13-2.10 (m, 2H).	98.6	525.2

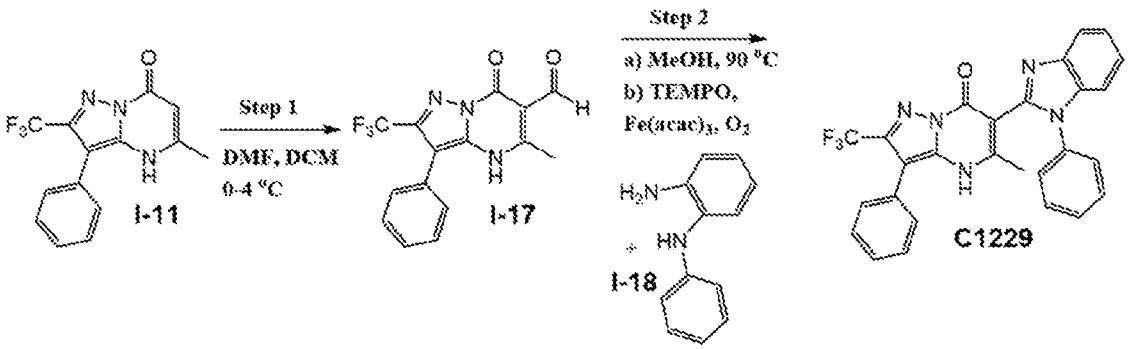
Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1264	 Also replace **I-1** with 	(500 MHz, DMSO) δ 11.94 (s, 1H), 7.28 – 7.19 (m, 4H), 7.19 – 7.13 (m, 1H), 3.87 (s, 2H), 2.40 (s, 3H), 1.72 – 1.65 (m, 1H), 0.97 – 0.91 (m, 2H), 0.61 – 0.56 (m, 2H).	99.6	348.1
C1265	 Also replace **I-1** with 	(500 MHz, DMSO) δ 12.13 (s, 1H), 7.45 (ddd, *J* = 7.6, 4.5, 1.2 Hz, 2H), 7.40 – 7.35 (m, 1H), 7.33 – 7.29 (m, 2H), 2.25 (s, 3H), 1.77 – 1.69 (m, 1H), 1.01 – 0.95 (m, 2H), 0.65 – 0.59 (m, 2H).	99.6	334.2
C1266	 Also replace **I-1** with 	(500 MHz, DMSO-d$_6$) δ 11.94 (s, 1H), 7.47 – 7.42 (m, 2H), 7.39 – 7.35 (m, 1H), 7.33 – 7.29 (m, 2H), 2.23 (s, 3H), 1.98 – 1.90 (m, 2H), 1.83 (dt, J = 9.3, 6.6 Hz, 2H), 1.71 (ddd, J = 26.5, 11.7, 6.7 Hz, 4H).	100	334.2

Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1267	 Also replace **I-1** with 	(500 MHz, DMSO-d_6) δ 11.78 (s, 1H), 7.27 – 7.21 (m, 4H), 7.19 – 7.14 (m, 1H), 3.87 (s, 2H), 3.30 – 3.21 (m, 1H), 2.39 (s, 3H), 1.96 – 1.87 (m, 2H), 1.86 – 1.77 (m, 2H), 1.74 – 1.60 (m, 4H).	100	376.2
C1268	 Also replace **I-1** with 	(500 MHz, DMSO-d_6) δ 11.77 (s, 1H), 7.28 – 7.21 (m, 4H), 7.19 – 7.14 (m, 1H), 3.87 (s, 2H), 3.35 – 3.27 (m, 1H), 2.39 (s, 3H), 1.29 (d, J = 7.1 Hz, 6H).	99.5	350.2
C1269	 Also replace **I-1** with 	(500 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.46 – 7.42 (m, 2H), 7.39 – 7.35 (m, 1H), 7.33 – 7.29 (m, 2H), 3.40 – 3.32 (m, 1H), 2.24 (s, 3H), 1.32 (d, J = 7.1 Hz, 6H).	99.9	336.1

Compound ID	Compound **I-16** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1280	 Also replace **I-1** with 	(500 MHz, DMSO) δ 8.14 (s, 1H), 7.98 – 7.84 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.1 Hz, 1H), 2.79 – 2.58 (m, 2H), 2.37 (s, 3H), 1.82 – 1.43 (m, 6H), 1.32 – 1.15 (m, 2H).	97.7	334.2

Example 6

[00433] Synthesis of 5-methyl-3-phenyl-6-(1-phenyl-1*H*-benzo[*d*]imidazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4H)-one (**C1229**) was carried out in two steps as follows:



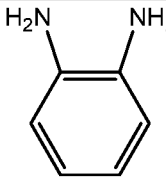
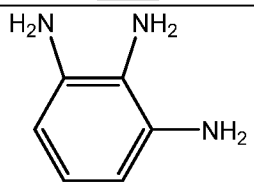
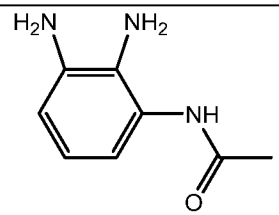
[00434] **Step 1**: Synthesis of 5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carbaldehyde (**I-17**): A suspension of 5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-11**, 1.00 g, 3.41 mmol) in dry DMF (3.40 mL), is pre-cooled to 0-4 °C using an ice/water bath. In a separate flask, oxalyl chloride (383 µL, 4.43 mmol) is dissolved in DCM (3.41 mL) and cooled to 0-4 °C using an ice/water bath. To this solution is added DMF (343 µL, 4.43 mmol) and the resulting mixture is added dropwise to the suspension of compound **I-11**. The reaction mixture is stirred at 0-4 °C and gradually warmed to room temperature. After overnight at room temperature, the reaction mixture is poured into a mixture of ice and 1M NaOH aqueous solution. EtOAc is then added and layers are separated. The organic layer is washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude oil was

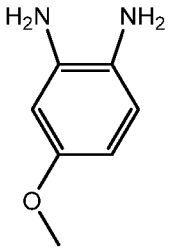
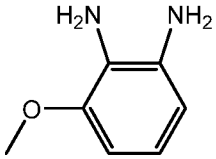
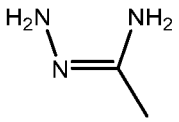
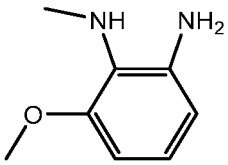
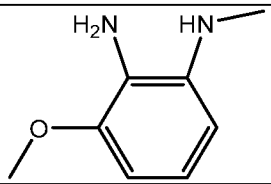
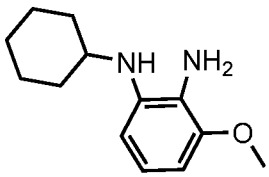
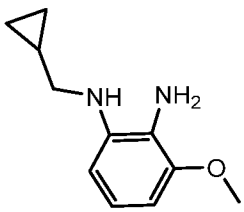
purified by normal phase chromatography (SiO_2, using a gradient of 0 to 20% MeOH in DCM) to afford the compound **I-17**. MS (m/z): 322.0 $[M+1]^+$, 92.25%.

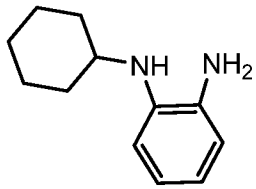
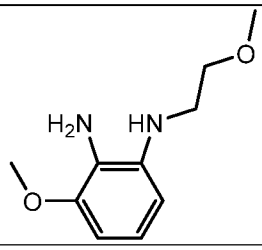
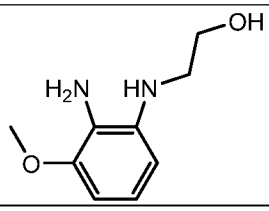
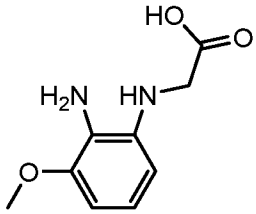
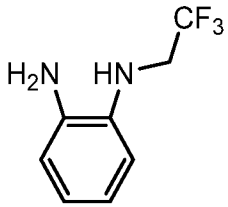
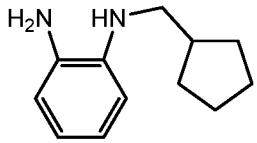
[00435] Step 2: Synthesis of 5-methyl-3-phenyl-6-(1-phenyl-1*H*-benzo[*d*]imidazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4H)-one (**C1229**): To a stirred solution of compound **I-17** (50 mg, 0.156 mmol) in MeOH (1 mL) was added *N*-phenylbenzene-1,2-diamine (**I-18**, 28.7 mg, 0.156 mmol). The reaction mixture was placed in a preheated oil bath at 90 °C overnight. After this time, reaction mixture was cooled to room temperature and TEMPO (2.5 mg, 0.016 mmol), followed by iron(III) acetylacetonate (11 mg, 0.031 mmol) were added. O_2 was bubbled into the dark solution for 5 min and the resulting mixture was heated at 40 °C for 2 h. After this time, the reaction mixture was concentrated *in vacuo* to dryness. The residue was purified by reverse flash chromatography (KP-C18- H5, using a gradient 0 to 100 MeCN/H_2O (0.1% ammonium formate buffer) to afford compound **C1229** after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 12.68 (s, 1H), 7.74 (d, J = 6.9 Hz, 1H), 7.55 – 7.33 (m, 10H), 7.32 – 7.11 (m, 3H), 2.21 (s, 3H); MS (m/z): 486.1 $[M+1]^+$, 99.4%.

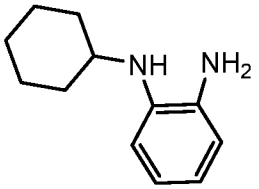
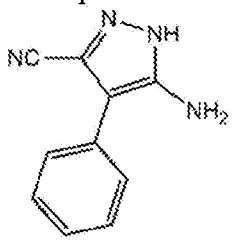
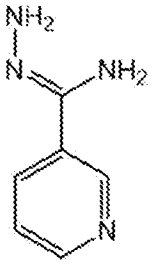
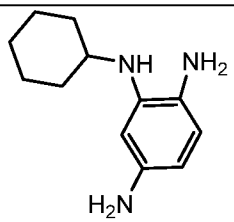
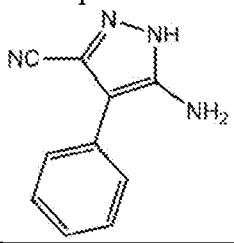
[00436] Table 7 below provides additional compounds that can be synthesized similarly to the methods described in steps 1-2 above, substituting the listed compound as indicated for **I-18**, as well as substituting for **I-1** (per Example 3) where indicated to give the suitable **I-11** analog. Data for compounds synthesized is provided in columns 3-5.

Table 7

Compound ID	Compound **I-18** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1005		(500MHz, DMSO) δ 12.99 (bs, 1H), 7.66 (bs, 2H), 7.60 (d, J = 7.5 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.25 (bs, 2H), 2.75 (s, 3H).	96.4	410.1
C1008		(500MHz, DMSO) δ 8.32 (s, 2H), 7.63 (d, J = 7.4Hz, 2H), 7.46 – 7.38 (m, 2H), 7.32 – 7.23 (m, 1H), 6.83 – 6.76 (m, 2H), 6.35 – 6.26 (m, 1H), 2.79 (s, 3H).	97.7	425.1
C1009		(500MHz, DMSO) δ 12.92 (s, 1H), 12.07 (s, 1H), 7.97 (s, 1H), 7.54 (d,J = 7.4Hz, 2H), 7.48 (t, J = 7.7Hz, 2H), 7.38 (t, J = 7.4Hz, 1H), 7.18 (dt, J = 15.7, 7.9Hz, 2H), 2.72 (s, 3H), 2.60 (s, 3H).	95.1	467.1

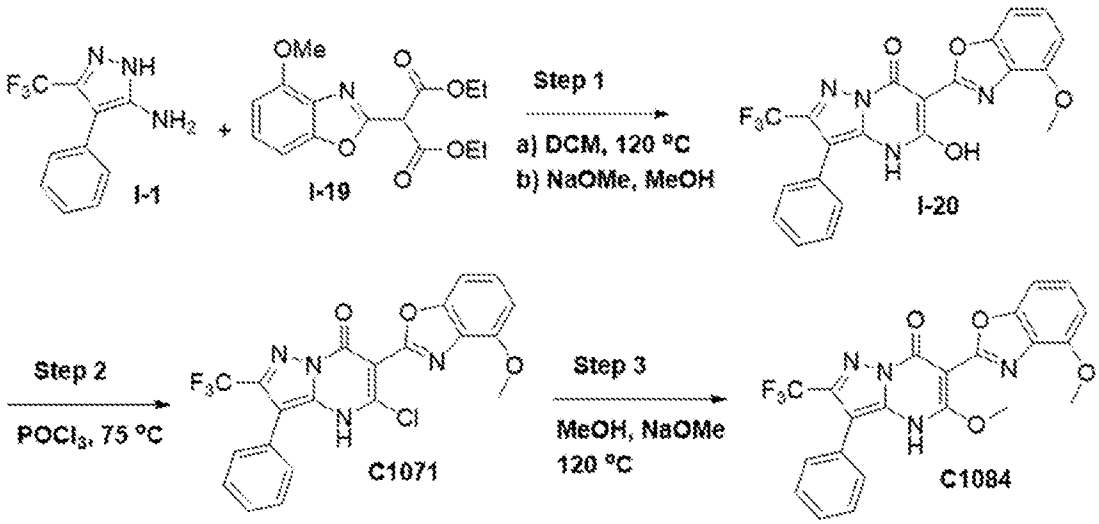
Compound ID	Compound **I-18** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1016		(500 MHz, DMSO) δ 12.89 (s, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.50 (d, J = 8.7 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.31 (t, J = 7.4 Hz, 1H), 7.18 (d, J = 2.3 Hz, 1H), 6.81 (d, J = 6.5 Hz, 1H), 3.80 (s, 3H), 2.76 (s, 3H).	96.5	440.3
C1018		(500 MHz, DMSO) δ 7.56 (d, J = 7.5 Hz, 2H), 7.49 (t, J = 7.5 Hz, 2H), 7.43 – 7.36 (m, 1H), 7.29 (s, 2H), 6.92 (br s, 1H), 4.01 (s, 3H), 2.60 (s, 3H).	99.3	440.2
C1020		(500 MHz, DMSO) δ 12.82 (brs, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.41 – 7.32 (m, 3H), 7.17 (d, J = 8.3 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.98 (dd, J = 6.6, 2.3 Hz, 1H), 4.01 (s, 3H), 3.78 (s, 3H).	92.3	375.2
C1065		(500 MHz, DMSO) δ 7.63 (d, J = 8.1 Hz, 2H), 7.42 (t, J = 7.0 Hz, 2H), 7.33 – 7.26 (m, 1H), 7.21 (d, J = 7.8 Hz, 1H), 7.09 – 7.05 (m, 1H), 6.80 – 6.74 (m, 1H), 3.94 (s, 3H), 3.80 (s, 3H), 2.11 (s, 3H).	94.1	454.2
C1087		(500 MHz, DMSO) δ 7.62 (d, J = 6.3 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.31 (s, 1H), 7.15 (s, 2H), 6.73 (s, 1H), 3.97 (s, 3H), 3.60 (s, 3H), 2.16 (s, 3H).	99.4	454.1
C1176		(500 MHz, DMSO) δ 12.72 (br s, 1H),7.58 (d, J = 7.6 Hz, 2H), 7.53 – 7.43 (m, 2H), 7.43 – 7.32 (m, 2H), 7.25 – 7.12 (m, 1H), 6.88 – 6.68 (m, 1H), 4.18 – 4.03 (m, 1H), 3.95 (s, 3H), 2.27 – 2.14 (m, 3H), 2.11 (s, 3H), 1.83 (d, J = 10.9 Hz, 1H), 1.76 (d, J = 9.5 Hz, 1H), 1.72 – 1.56 (m, 2H), 1.41 – 1.18 (m, 3H).	98.05	522.0
C1189		(500 MHz, DMSO) δ 8.25 (s, 1H), 7.64 (d, J = 7.3 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.31 – 7.24 (m, 1H), 7.22 – 7.16 (m, 1H), 7.12 (t, J = 8.0 Hz, 1H), 6.70 (d, J = 7.2 Hz, 1H), 4.07 – 3.98 (m, 1H), 3.96 (s, 3H), 3.86 – 3.74 (m, 1H), 2.11 (s, 3H), 1.10 – 1.01 (m, 1H), 0.41 – 0.30 (m, 2H), 0.30 – 0.22 (m, 1H), 0.13 – 0.03 (m, 1H).	99.37	494.0

Compound ID	Compound **I-18** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1190		(500 MHz, DMSO) δ 12.74 (s, 1H), 8.09 – 7.86 (m, 1H), 7.77 – 7.64 (m, 1H), 7.61 – 7.47 (m, 4H), 7.46 – 7.20 (m, 3H), 4.29 – 4.12 (m, 1H), 2.33 – 2.09 (m, 6H), 1.92 – 1.80 (m, 1H), 1.82 – 1.70 (m, 2H), 1.69 – 1.53 (m, 1H), 1.47 – 1.17 (m, 3H).	99.69	492.1
C1200		(500 MHz, DMSO) δ 12.81 (s, 1H), 7.76 – 7.11 (m, 7H), 7.03 – 6.63 (m, 1H), 4.57 – 4.10 (m, 2H), 3.98 (s, 3H), 3.73 – 3.55 (m, 1H), 3.53 – 3.41 (m, 1H), 3.08 (s, 3H), 2.20 (s, 3H).	99.9	498.0
C1201		(500 MHz, DMSO) δ 12.77 (s, 1H), 7.72 – 7.13 (m, 7H), 7.04 – 6.63 (m, 1H), 4.89 – 4.64 (m, 1H), 4.40 – 4.04 (m, 2H), 3.98 (s, 3H), 3.73 – 3.49 (m, 2H), 2.22 (s, 3H).	98.48	484.0
C1221		(500 MHz, DMSO) δ 13.13 (s, 2H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.52 – 7.44 (m, 2H), 7.43 – 7.33 (m, 1H), 7.26 – 7.05 (m, 2H), 6.87 – 6.69 (m, 1H), 5.17 – 4.72 (m, 2H), 3.97 (s, 3H), 2.20 (s, 3H).	99.9	498.1
C1231		(500 MHz, DMSO) δ 12.83 (s, 1H), 7.80 – 7.68 (m, 2H), 7.63 – 7.44 (m, 5H), 7.43 – 7.24 (m, 2H), 5.53 – 5.29 (m, 1H), 5.15 – 4.91 (m, 1H), 2.22 (s, 3H).	98.47	492.1
C1235		(500 MHz, DMSO) δ 7.86 – 7.76 (m, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.53 – 7.45 (m, 2H), 7.44 – 7.29 (m, 3H), 4.30 – 4.22 (m, 1H), 4.14 – 4.03 (m, 1H), 2.39 – 2.29 (m, 1H), 2.22 (s, 3H), 1.61 – 1.33 (m, 6H), 1.22 – 0.99 (m, 2H).	96.92	492.2

Compound ID	Compound **I-18** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1276	 Also replace **I-1** with 	(500 MHz, DMSO) δ 8.36 – 7.75 (m, 4H), 7.72 – 7.26 (m, 5H), 4.29 (br s, 1H), 4.19 – 3.81 (m, 3H), 2.32 – 2.19 (m, 4H), 1.89 – 1.74 (m, 2H), 1.68 – 1.59 (m, 1H), 1.45 – 1.22 (m, 3H).	100	449.2
C1278		(500 MHz, DMSO) δ 8.40 (s, 1H), 7.81 – 7.56 (m, 2H), 7.47 (s, 1H), 6.75 – 6.45 (m, 5H), 1.88 (s, 3H).	97.2	438.1
C1279	 Also replace **I-1** with 	(500 MHz, MeOD) δ 7.85 – 7.81 (m, 2H), 7.41 – 7.33 (m, 3H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 1.8 Hz, 1H), 6.77 (dd, *J* = 8.7, 1.9 Hz, 1H), 4.11 – 4.02 (m, 1H), 2.25 – 2.19 (m, 2H), 2.13 (s, 3H), 1.84 – 1.68 (m, 4H), 1.34 – 1.22 (m, 4H).	95.2	464.3

Example 7

[00437] Synthesis of 5-chloro-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1071**) and 5-methoxy-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1084**) were carried out in two and three steps, respectively, as follows:



[00438] Step 1: Synthesis of 5-hydroxy-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-20**): A mixture of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine (**I-1**, 1.68 g, 7.40 mmol) and 2-(4-methoxybenzo[d]oxazol-2-yl)malonate (**I-19**, 2.50 g, 8.14 mmol) were dissolved in DCM (5 mL). The reaction mixture was concentrated *in vacuo* and the residue was heated at 120 °C for 2 h. LCMS showed complete reaction and the crude mixture was dissolved in MeOH (5 mL), and sodium methoxide in MeOH (30 mmol) was added and the reaction was stirred at r.t. for 3 h. The reaction was quenched with AcOH, and concentrated *in vacuo*. The desired compound was crashed out after adding water. The resulting white solid was filtered and dried *in vacuo* to afford compound **I-20**. MS (m/z): 443.0 $[M+1]^+$.

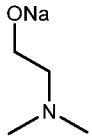
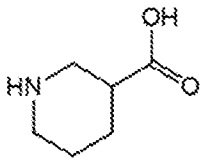
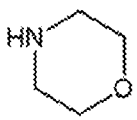
[00439] Step 2: Synthesis of 5-chloro-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1071**): Compound **I-20** (2.0 g, 4.52 mmol) was dissolved in $POCl_3$ (10 mL) and heated at 75 °C for 4 h in a sealed tube. The excess $POCl_3$ was removed *in vacuo* and the crude material was purified directly on normal phase flash chromatography (Hexanes:EtOAc, 100:10 to 0:100) to obtain compound **C1071**. MS (m/z): 460.8 $[M+1]^+$.

[00440] Step 3: Synthesis of 5-methoxy-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1084**): Sodium methoxide (0.05 mL of 25% in MeOH, 0.217 mmol) was added to a solution of compound **C1071** (10 mg, 0.0217mmol) dissolved in MeOH (1.0 mL, alternatively DMF can be used here depending on the desired compound) with stirring, then heated at 120 °C for 1 h. The reaction mixture was quenched with sat. NH_4Cl, diluted with EtOAc (5 mL), and the two phases were separated. The organic layer was washed with Sat. NH_4Cl, then brine and dried over Na_2SO_4. The

mixture was concentrated *in vacuo* and purified by reverse phase chromatography using MeCN/H2O (0.1% ammonium formate buffer) as the eluent to afford compound **C1084**. ^{1}H NMR (500 MHz, DMSO) δ 7.66 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.29 (m, 3H), 6.98 – 6.94 (m, 1H), 4.00 (s, 3H), 3.83 (s, 3H). MS (m/z): 457.1 $[M+1]^+$, 96.0%.

[00441] Table 8 below provides additional compounds that can be synthesized similarly to the methods described in step 3 above, substituting the listed compound for NaOMe in Step 3. Data for compounds synthesized is provided in columns 3-5.

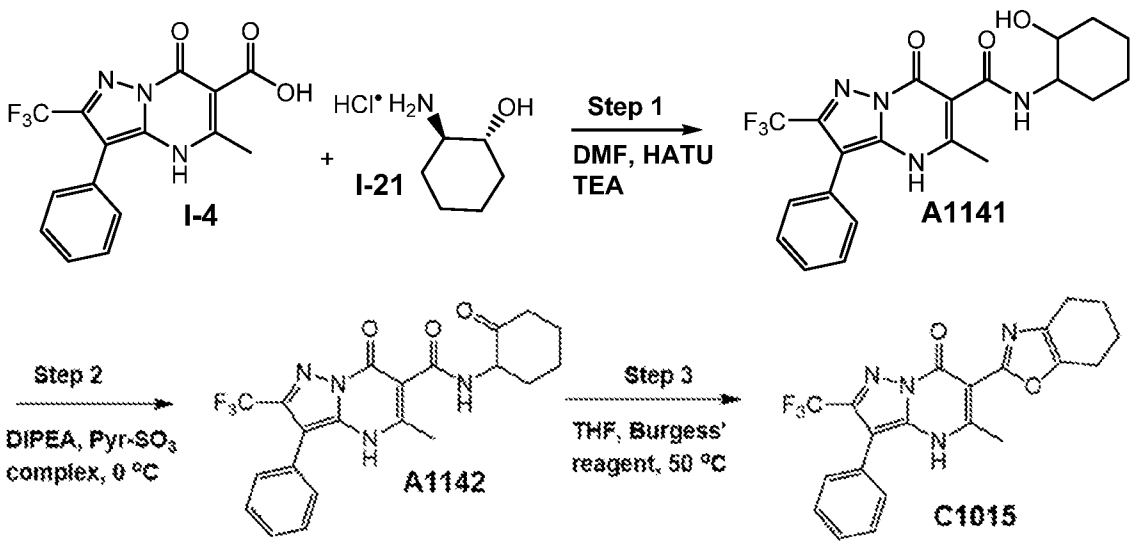
Table 8

Compound ID	NaOMe replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1067		(400 MHz, DMSO) δ 7.63 (d, J = 7.8 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.32 – 7.23 (m, 3H), 6.92 (d, J = 7.5 Hz, 1H), 4.56 (t, J = 5.1 Hz, 2H), 3.99 (s, 3H), 3.18 (s, 2H), 2.67 (s, 6H).	96.6	514.9
C1085	NH_3	(500 MHz, DMSO) δ 8.15 (s, 1H), 7.58 (d, J = 7.3 Hz, 2H), 7.37 (t, J = 7.8 Hz, 2H), 7.27 – 7.19 (m, 2H), 7.15 (d, J = 8.1 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 3.96 (s, 3H).	94.0	442.0
C1121	NaSMe	(500 MHz, DMSO) δ 7.72 (d, J = 7.5 Hz, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.29 – 7.24 (m, 3H), 6.90-6.88 (m, 1H), 4.02 (s, 3H), 2.37 (s, 3H).	97.8	472.9
C1257		(500 MHz, DMSO) δ 7.73 (d, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.26 – 7.18 (m, 3H), 6.86 (dd, *J* = 6.5, 2.4 Hz, 1H), 3.98 (s, 3H), 3.82 (d, *J* = 11.2 Hz, 1H), 2.75 – 2.68 (m, 1H), 2.62 (d, *J* = 11.9 Hz, 1H), 1.89 -1.84 (m, 1H), 1.44-1.36 (m, 3H).	99.9	554.2
C1258		500 MHz, DMSO) δ 7.67 (d, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.26 – 7.21 (m, 3H), 6.88 (dd, *J* = 7.0, 2.0 Hz, 1H), 3.99 (s, 3H), 3.50 – 3.46 (m, 4H), 3.06 – 3.02 (m, 4H).	99.9	512.2

Example 8

[00442] Synthesis of *N*-(2-hydroxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1141**), 5-methyl-7-oxo-*N*-(2-oxocyclohexyl)-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1142**), and 5-methyl-3-phenyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-2-

(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1015**) were carried out in one, two and three steps, respectively, as follows:



[00443] Step 1: Synthesis of *N*-(2-hydroxycyclohexyl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1141**): To a mixture of 5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxylic acid (**I-4,** 50.0 mg, 148 μmol), trans-2-aminocyclohexanol hydrochloride (**I-21**, 45.0 mg, 297 μmol), HATU (58.1 mg, 148 μmol) in DMF (740 μL) was added TEA (83.5 μL, 593 μmol) and the solution was stirred at r.t. for 24h. Afterwards, the reaction mixture was purified directly on a reverse flash chromatography (KP-C18-H5, using a gradient 0 to 100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **A1141** as a white solid after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 12.53 (s, 1H), 7.55 – 7.39 (m, 5H), 4.65 (s, 1H), 3.68 – 3.52 (m, 1H), 3.37 – 3.31 (m, 1H), 2.51 (s, 3H), 1.98 – 1.91 (m, 1H), 1.89 – 1.82 (m, 1H), 1.68 – 1.56 (m, 2H), 1.33 – 1.15 (m, 4H); MS (m/z): 435.3 $[M+1]^+$.

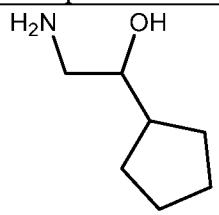
[00444] Step 2: Synthesis of 5-methyl-7-oxo-*N*-(2-oxocyclohexyl)-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1142**): To a solution of compound **A1141** (50.0 mg, 115 μmol) in DIPEA (241 μL, 1.37 mmol) was added sulfur trioxide pyridine complex (220 mg, 1.38 mmol) followed by DIPEA (241 μL, 1.37 mmol) at 0 °C. The reaction was gradually warmed to r.t. overnight. After 18h, the reaction mixture was diluted with 1N HCl (10 mL) and extracted with EtOAc (3 x 10 mL). The organic fraction was washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude reaction mixture was directly subjected to purification via

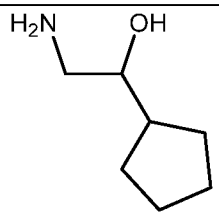
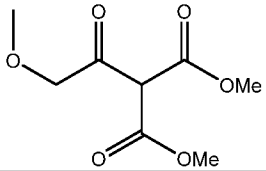
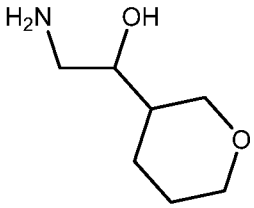
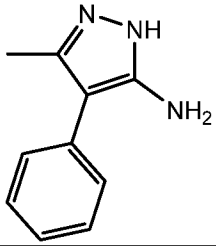
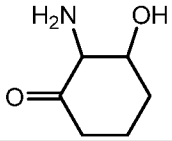
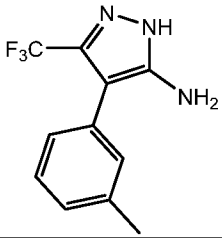
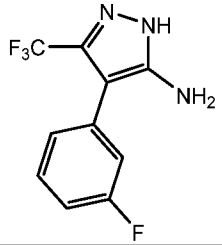
reverse flash chromatography (KP-C18-H5, using a gradient 0 to 100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **A1142** (22.5 mg, 45 %) as a white solid after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 12.71 (s, 1H), 7.55 (d, J = 7.2 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.31 (s, 1H), 4.60 (dt, J = 12.3, 6.2 Hz, 1H), 2.59 (s, 3H), 2.47 – 2.38 (m, 2H), 2.38 – 2.28 (m, 1H), 2.08 – 1.99 (m, 1H), 1.87 – 1.73 (m, 2H), 1.62 (s, 1H), 1.50 – 1.39 (m, 1H). MS (m/z): 433.1 $[M+1]^+$, 96.9%.

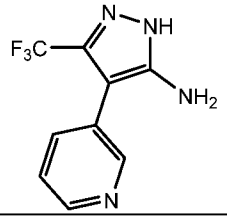
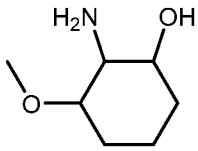
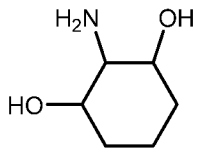
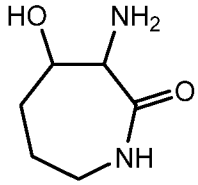
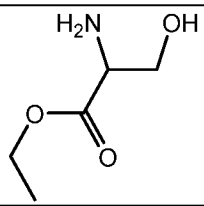
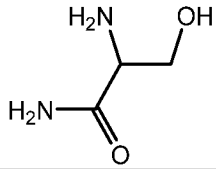
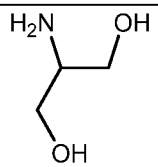
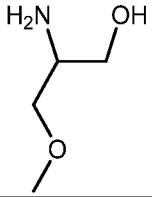
[00445] Step 3: Synthesis of 5-methyl-3-phenyl-6-(4,5,6,7-tetrahydrobenzo[*d*]oxazol-2-yl)-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1015**): To a 10 mL flask containing compound **A1142** (21.5 mg, 49.7 µmol) in THF (2.50 mL) was added Burgess reagent (30.6 mg, 124 µmol). The resulting solution was stirred overnight at 50 °C. Additional Burgess reagent (61.4 mg, 249 µmol) was added and stirred until full consumption of starting material. Afterwards, the crude solution was directly subjected to purification via reverse flash chromatography (KP-C18-H5, using a gradient 0 to 100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **C1015** after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 8.41 (s, 2H), 7.58 (d, J = 7.4 Hz, 2H), 7.43 – 7.37 (m, 2H), 7.29 – 7.23 (m, 1H), 2.67 – 2.60 (m, 2H), 2.50 – 2.46 (m, 2H), 2.18 (s, 3H), 1.87 – 1.74 (m, 4H).MS (m/z): 415.2 $[M+1]^+$, 97.9%.

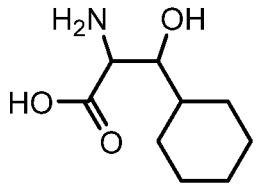
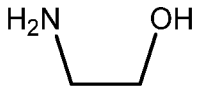
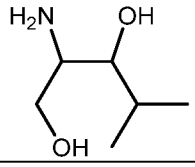
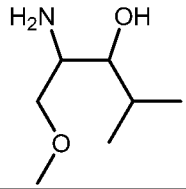
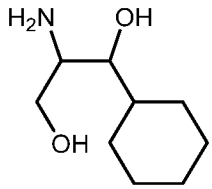
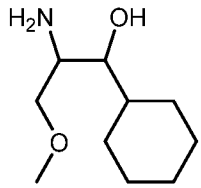
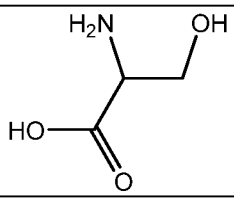
[00446] Table 9 below provides additional compounds that can be synthesized similarly to the methods described in steps 1-3 above, optionally substituting the listed compound for **I-21**, and/or substituting for **I-1** and/or **I-2** (see Example 1) where indicated to provide the suitable analog of for **I-4**. Data for compounds synthesized is provided in columns 3-5.

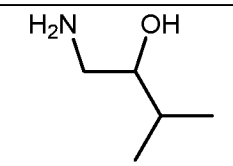
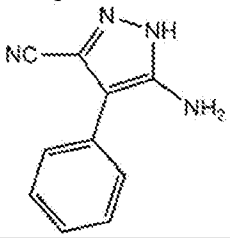
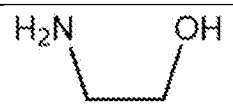
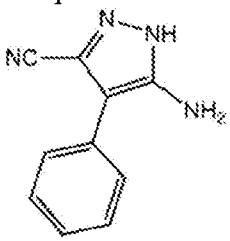
Table 9

Compound ID	Compound **I-21** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1010		(500 MHz, DMSO) δ 7.55 – 7.40 (m, 5H), 7.02 (s, 1H), 3.24 – 3.16 (m, 1H), 2.38 – 2.29 (m, 3H), 2.05 – 1.95 (m, 2H), 1.76 – 1.59 (m, 6H).	95.5	429.9

C1013	 Also replace **I-2** with 	(500 MHz, DMSO) δ 7.53 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.7 Hz, 2H), 7.21 (t, J = 7.5 Hz, 1H), 6.78 (s, 1H), 4.20 (s, 2H), 3.09 (s, 1H), 3.02 (s, 3H), 1.97 – 1.87 (m, 2H), 1.70 – 1.49 (m, 6H).	100	459.2
C1027		(500 MHz, DMSO) δ 12.73 (s, 1H), 7.52 (d, J = 7.4 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.39 (d, J = 7.3 Hz, 1H), 7.03 (s, 1H), 3.98 (dd, J = 10.9, 2.9 Hz, 1H), 3.80 (dt, J = 11.7, 3.7 Hz, 1H), 3.48 – 3.40 (m, 2H), 3.05 – 2.97 (m, 1H), 2.28 (s, 3H), 2.12 – 2.04 (m, 1H), 1.79 – 1.59 (m, 3H).	97.7	445.1
C1032	Replace **I-1** with 	(500 MHz, DMSO) δ 7.68 (d, J = 6.5 Hz, 2H), 7.41 (t, J = 7.7 Hz, 2H), 7.23 (d, J = 7.5 Hz, 1H), 2.67-2.61 (m, 2H), 2.50-2.47 (m, 2H), 2.39 (s, 3H), 2.26 (s, 3H), 1.88-1.75 (m, 4H).	99.2	361.2
C1033		(500 MHz, DMSO) δ 7.54 – 7.36 (m, 5H), 3.05 (t, J = 6.2 Hz, 2H), 2.55 – 2.51 (m, 2H), 2.36 (s, 3H), 2.21 – 2.13 (m, 2H).	96.8	429.2
C1034	Replace **I-1** with 	(500MHz, DMSO) δ 12.74 (brs, 1H), 7.35-7.30 (m, 3H), 7.18-7.17 (m, 1H), 2.66-2.64 (m, 2H), 2.36 (s, 3H), 2.28 (brs, 2H), 1.88-1.75 (m, 4H).	100	429.2
C1035	Replace **I-1** with 	(500MHz, DMSO) δ 12.77 (brs, 1H), 7.50-7.46 (m, 3H), 7.15-7.08 (m, 1H), 3.18(d, J = 5.1 Hz, 2H), 2.69-2.62 (m, 2H), 2.22 (s, 3H), 1.87-1.76 (m, 4H).	97.0	433.4

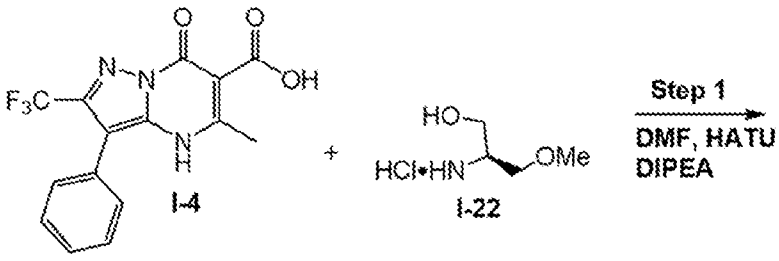
C1036	Replace **I-1** with 	(500MHz, DMSO) δ 8.80 (s, 1H), 8.46 (d, J = 3.6 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.45 (dd, J = 7.9, 4.7 Hz, 1H), 2.64 (m, 2H), 2.20 (s, 3H), 1.88-1.76 (m, 4H), 1.27-1.21 (m, 2H).	98.9	416.6
C1048		(500 MHz, DMSO) δ 12.67 (s, 1H), 7.49 (d, J = 7.5 Hz, 2H), 7.37 (t, J = 7.7 Hz, 2H), 7.26 (t, J = 7.1 Hz, 1H), 4.20 (t, J = 3.5 Hz, 1H), 3.34 (s, 3H), 2.64 (ddd, J = 16.5, 5.7, 3.4 Hz, 1H), 2.59 – 2.50 (m, 1H), 2.19 (s, 3H), 1.94 – 1.80 (m, 2H), 1.80 – 1.64 (m, 2H).	99.6	445.3
C1052		(500 MHz, DMSO) δ 7.59 (d, J = 7.4 Hz, 2H), 7.42 – 7.37 (m, 2H), 7.28 – 7.23 (m, 1H), 5.02 (d, J = 5.6 Hz, 1H), 4.56 (d, J = 4.6 Hz, 1H), 2.70 – 2.62 (m, 1H), 2.60 – 2.56 (m, 1H), 2.20 (s, 3H), 2.03 – 1.95 (m, 1H), 1.85 – 1.72 (m, 3H).	98.0	431.2
C1059		(400 MHz, DMSO) δ 7.89 (s, 1H), 7.54 (d, J = 7.5 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.36 (t, J = 7.1 Hz, 1H), 3.25 (dd, J = 9.1, 5.6 Hz, 2H), 3.03 (t, J = 6.5 Hz, 2H), 2.32 (s, 3H), 1.99 (dd, J = 14.4, 6.0 Hz, 2H).	95.1	444.2
C1101		(500 MHz, DMSO) δ 12.93 (s, 1H), 8.89 (s, 1H), 7.52 (m, 2H), 7.47 (m, 2H), 7.38 (m, 1H), 4.31 (q, J = 7.1 Hz, 2H), 2.33 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H).	99.0	433.0
C1102		(500 MHz, DMSO) δ 8.52 (s, 1H), 7.63 – 7.56 (m,2H), 7.41 (t, J = 6.8 Hz, 2H), 7.28 (t, J = 6.8 Hz, 1H), 7.07 (bs, 2H), 2.25 (s, 3H).	98.9	404.1
C1104		(500 MHz, DMSO) δ 7.91 (s, 1H), 7.55 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.32 (s, 1H), 5.17 (s, 1H), 4.42 (d, J = 4.7 Hz, 2H), 2.25 (s, 3H).	98.5	391.1
C1108		(500 MHz, DMSO) δ 7.58 (d, J = 7.5 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.29 – 7.24 (m, 1H), 4.34 (d, J = 0.6 Hz, 2H), 3.31 (s, 3H), 2.20 (s, 3H).	99.7	405.1

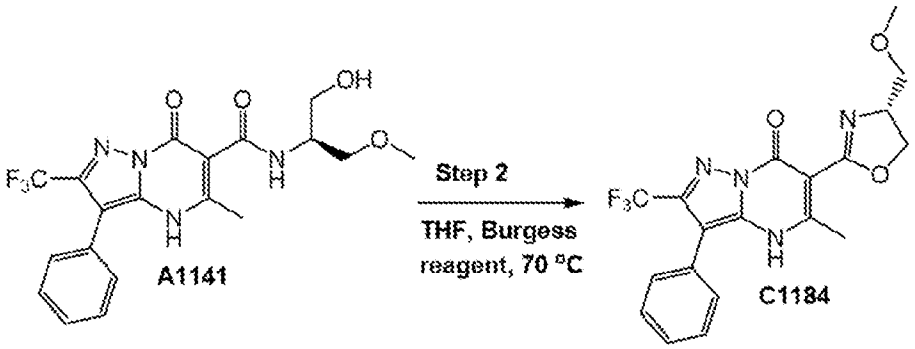
C1169		(500 MHz, DMSO) δ 12.84 (s, 1H), 7.54 (d, J = 7.5 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.40 – 7.28 (m, 1H), 3.48 – 3.41 (m, 1H), 2.26 (s, 3H), 1.90 – 1.76 (m, 4H), 1.69 (d, J = 12.3 Hz, 1H), 1.59 – 1.48 (m, 2H), 1.40 – 1.22 (m, 3H).	100	487.0
C1170		(500 MHz, DMSO) δ 8.12 (s, 1H), 7.56 (d, J = 7.7 Hz, 2H), 7.47 – 7.41 (m, 2H), 7.34 – 7.25 (m, 2H), 2.23 (s, 3H).	100	361.0
C1143		(400 MHz, DMSO-d6) δ 7.50 – 7.40 (m, 4H), 7.39 – 7.31 (m, 1H), 4.96 (s, 1H), 4.35 (s, 2H), 3.24 – 3.14 (m, 1H), 2.25 (s, 3H), 1.21 (d, J = 6.9 Hz, 6H).	97.1	433.1
C1153		(500 MHz, MeOD) δ 7.51 (d, J = 7.2 Hz, 2H), 7.47 – 7.42 (m, 2H), 7.39 – 7.35 (m, 1H), 4.43 (s, 2H), 3.39 (s, 3H), 3.28 – 3.21 (m, 1H), 2.32 (s, 3H), 1.34 (d, J = 6.9 Hz, 6H).	99.3	447.1
C1157		(500 MHz, MeOD) δ 7.51 (d, J = 7.2 Hz, 2H), 7.46 – 7.41 (m, 2H), 7.39 – 7.34 (m, 1H), 4.55 (s, 2H), 2.92 (dddd, J = 12.0, 12.0, 3.5, 3.5 Hz, 1H), 2.33 (s, 3H), 1.98 – 1.90 (m, 2H), 1.90 – 1.83 (m, 2H), 1.79 – 1.72 (m, 1H), 1.71 – 1.60 (m, 2H), 1.51 – 1.39 (m, 2H), 1.38 – 1.26 (m, 1H).	100	473.1
C1158		(400 MHz, MeOD) δ 7.53 – 7.48 (m, 2H), 7.44 – 7.38 (m, 2H), 7.36 – 7.31 (m, 1H), 4.71 (s, 2H), 3.82 (s, 3H), 3.04 (tt, J = 11.9, 3.4 Hz, 1H), 2.37 (s, 3H), 2.00 – 1.91 (m, 2H), 1.91 – 1.82 (m, 2H), 1.80 – 1.71 (m, 1H), 1.69 – 1.58 (m, 2H), 1.52 – 1.39 (m, 2H), 1.37 – 1.26 (m, 1H).	99.6	487.2
C1165		(500 MHz, MeOD) δ 8.44 (s, 1H), 7.54 – 7.37 (m, 5H), 2.46 (s, 3H).	95.2	405.0

C1260	 Replace **I-1** with 			
C1270	 Replace **I-1** with 	(500 MHz, DMSO) δ 8.26 (s, 1H), 7.69 (s, 2H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.41 (s, 1H), 2.41 (s, 3H).	97.7	318.1

Example 9

[00447] Synthesis of (*S*)-*N*-(1-hydroxy-3-methoxypropan-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1143**), and (*R*)-6-(4-(methoxymethyl)-4,5-dihydrooxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1184**) were carried out in one and two steps, respectively, as follows:



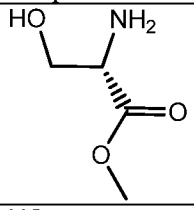
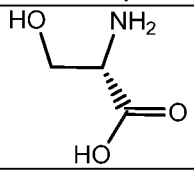
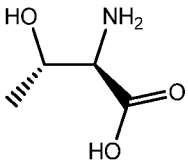
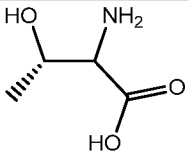


[00448] Step 1: Synthesis of (*S*)-*N*-(1-hydroxy-3-methoxypropan-2-yl)-5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxamide (**A1143**): A solution of 5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-6-carboxylic acid (**I-4**, see Example 1, 1.00 g, 2.97 mmol), HATU (4.51 g, 11.9 mmol) and *N,N*-diisopropylethylamine (2.61 mL, 14.8 mmol) in DMF (319 µL) was stirred for 30 min. L-serine methyl ether hydrochloride (**I-22**, 840 mg, 5.93 mmol) was added. The resulting solution was stirred at r.t. for 1h. 1N HCl was added and the mixture was extracted with EtOAc (3 x 20 mL). The organic layer was washed with sat NH_4Cl (10 mL), then brine (10 mL) and dried over Na_2SO_4, filtered and concentrated to afford compound **A1143**. MS (m/z): 425.0 $[M+1]^+$.

[00449] Step 2: Synthesis of (*R*)-6-(4-(methoxymethyl)-4,5-dihydrooxazol-2-yl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1184**): To a 10 mL flask containing compound **A1143** (30.0 mg, 70.7 µmol) in THF (1.18 mL) was added Burgess reagent (20.9 mg, 84.8 µmol). The resulting solution was stirred overnight at 70 °C. Afterwards, the reaction mixture was diluted in saturated ammonium chloride (10 mL) and extracted with EtOAc (3 x 20 mL). The organic phase was washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The product was stored in a minimal amount of EtOAc overnight. The precipitate that formed was filtered and washed with EtOAc, followed by drying to afford compound **C1184**. ^1H NMR (500 MHz, DMSO) δ 11.20 (s, 1H), 7.57 – 7.51 (m, 2H), 7.51 – 7.42 (m, 2H), 7.41 – 7.31 (m, 1H), 4.96 – 4.89 (m, 1H), 5.00 – 4.87 (m, 1H), 4.75 (dd, J = 8.8, 6.0 Hz, 1H), 4.56 – 4.50 (m, 1H), 3.69 (dd, J = 10.1, 3.9 Hz, 1H), 3.57 (dd, J = 10.2, 3.5 Hz, 1H), 3.32 (s, 3H), 2.52 (s, 3H). MS (m/z): 407.1 $[M+1]^+$, 100%.

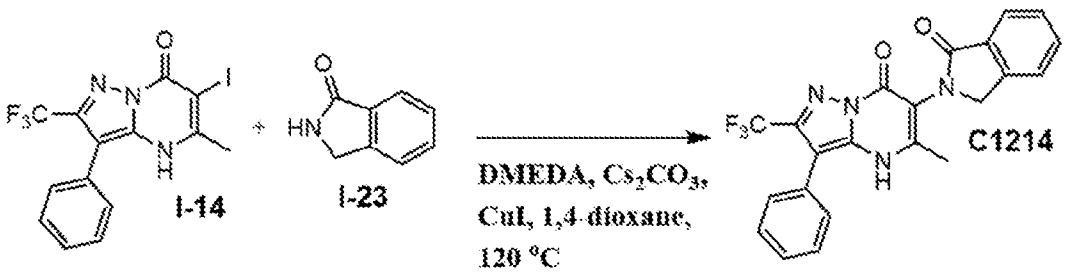
[00450] Table 10 below provides additional compounds that can be synthesized similarly to the methods described in steps 1-2 above, substituting the listed compound for **I-22**. Data for compounds synthesized is provided in columns 3-5.

Table 10

Compound ID	Compound **I-22** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1187		(400 MHz, DMSO) δ 11.43 (s, 1H), 7.55 – 7.50 (m, 2H), 7.49 – 7.42 (m, 2H), 7.40 – 7.34 (m, 1H), 5.10 – 4.97 (m, 3H), 3.76 (s, 3H), 2.51 – 2.50 (m, 3H)	95.6	421.0
C1192		(400 MHz, DMSO-d6) δ 11.34 (s, 1H), 7.55 – 7.50 (m, 2H), 7.50 – 7.43 (m, 2H), 7.41 – 7.33 (m, 1H), 5.15 – 5.01 (m, 2H), 4.97 (dd,J = 10.6, 5.4 Hz, 1H), 2.53 (s, 3H).	99.3	407.1
C1213		(500 MHz, DMSO) δ 7.53 (d, *J* = 7.4 Hz, 2H), 7.47 – 7.42 (m, 2H), 7.37 – 7.32 (m, 1H), 5.48 – 5.38 (m, 1H), 5.00 (d, *J* = 9.7 Hz, 1H), 3.76 (s, 3H), 2.49 (s, 3H), 1.41 (d, *J* = 6.5 Hz, 3H).	98.0	435.0
C1216		(400 MHz, DMSO) δ 7.54 (d, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 5.42 – 5.05 (m, 1H), 4.64 – 4.12 (m, 1H), 2.48 (s, 3H), 1.59 – 1.42 (m, 3H).	100 (3:1 dr)	421.0

Example 10

[00451] Synthesis of 5-methyl-6-(1-oxoisoindolin-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1214**) was carried out in one step as follows:

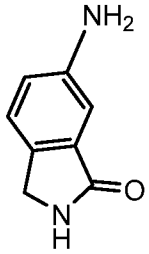
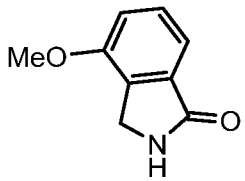


[00452] **Step 1**: To a sealed tube was added 1-isoindolinone (**I-23**, 32.4 mg, 239 µmol), *N,N'*-dimethylethylenediamine (27.0 µL, 239 µmol), Cs_2CO_3 (236 mg, 716 µmol), copper iodide (22.7 mg, 119 µmol), and was flushed with nitrogen. Afterwards, 1,4-dioxane (2.39 mL) and 6-iodo-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-14**, 100 mg, 239 µmol) were added. The mixture was bubbled with nitrogen for 5 min. The reaction was then heated at 120 °C overnight. The crude mixture was concentrated *in vacuo*, then subjected to purification via reverse flash chromatography (KP-C18-H5, using a gradient 0 to

100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **C1214** as a white solid after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 12.69 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.60 – 7.54 (m, 1H), 7.54 – 7.47 (m, 4H), 7.45 – 7.39 (m, 1H), 4.89 (d, *J* = 17.2 Hz, 1H), 4.60 (d, *J* = 17.2 Hz, 1H), 2.24 (s, 3H); MS (m/z): 425.1 $[M+1]^+$, 99.7%.

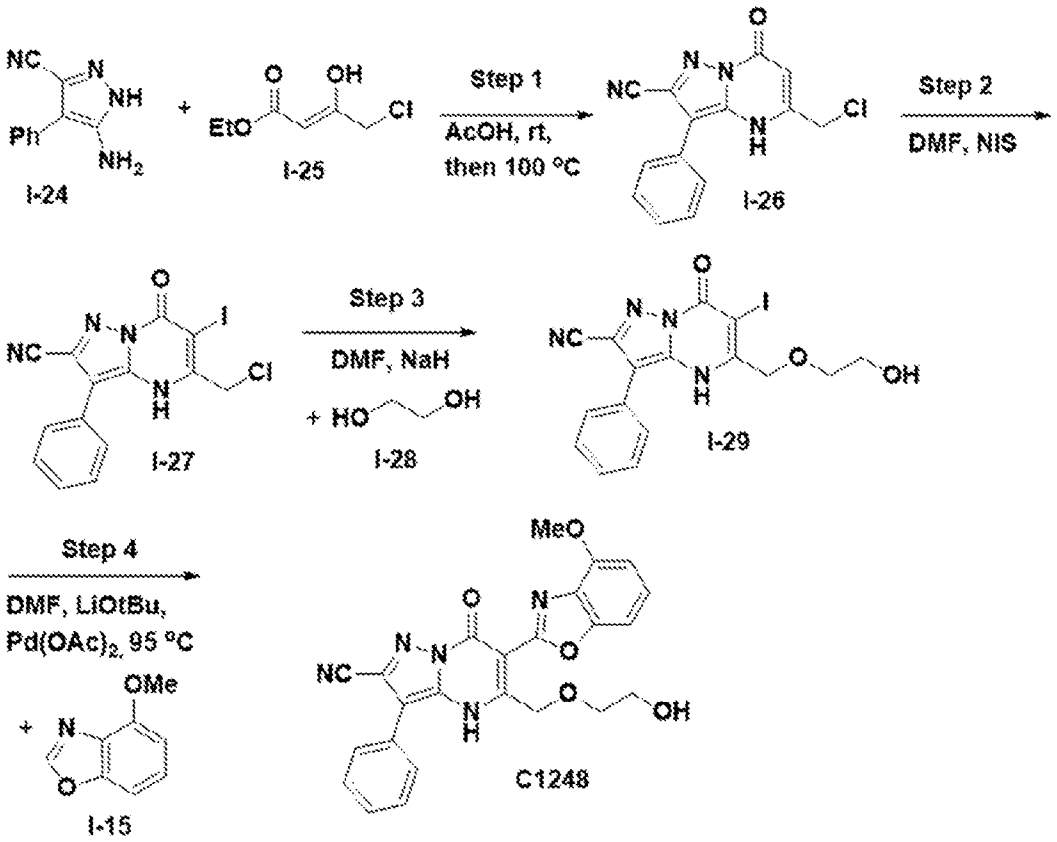
[00453] Table 11 below provides additional compounds that can be synthesized similarly to the methods described in the above step, substituting the listed compound for **I-23**. Data for compounds synthesized is provided in columns 3-5.

Table 11

Compound ID	Compound **I-23** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1217		(400 MHz, DMSO) δ 7.55 (d, *J* = 7.4 Hz, 2H), 7.49 – 7.41 (m, 2H), 7.38 – 7.31 (m, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 6.91 (s, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 5.32 (brs, 2H), 4.70 (d, *J* = 15.5 Hz, 1H), 4.34 (d, *J* = 15.6 Hz, 1H), 2.15 (s, 3H).	98.9	440.0
C1220		(500 MHz, DMSO) δ 12.68 (s, 1H), 7.58 – 7.45 (m, 5H), 7.44 – 7.35 (m, 2H), 7.30 (d, *J* = 8.1 Hz, 1H), 4.75 (d, *J* = 17.3 Hz, 1H), 4.52 (d, *J* = 17.4 Hz, 1H), 3.93 (s, 3H), 2.22 (s, 3H).	98.9	455.1

Example 11

[00454] Synthesis of 5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1248**) was carried out in four steps as follows:



[00455] Step 1: Synthesis of 5-(chloromethyl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**I-26**): Ethyl 4-Chloroacetoacetate (**I-25**, 927 µL, 6.51 mmol) was added to a solution of 5-amino-4-phenyl-1H-pyrazole-3-carbonitrile (**I-24,** 1.00 g, 4.34 mmol) in AcOH (4.93 mL). The solution was stirred at r.t. for 15 min and then heated at 100 °C for 1h. After cooling, the white suspension was filtered and the resulting solid was washed with Et_2O (x3) to provide the compound **I-26** as a beige solid. MS (m/z): $[M+H]^+$ 285.0.

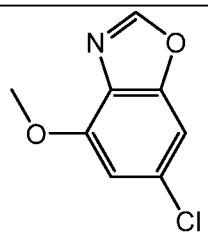
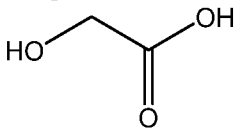
[00456] Step 2: Synthesis of 5-(chloromethyl)-6-iodo-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**I-27**): In a 20 mL microwave-vial was added compound **I-26** (500 mg, 1.76 mmol) in DMF (11.7 mL). N-iodosuccinimide (489 mg, 2.11 mmol) was then added in one portion. The reaction was stirred at r.t. for 20 min. The reaction was quenched with water and transferred in a separation funnel. The organic layer was separated and the aqueous layer was extracted (x2) with EtOAc. The combined organic layers were successively washed with aqueous thiosulfate solution (5%) and brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The product was triturated with a 1:1 mixture of diethyl ether:hexanes to afford compound **I-27** as a light brown solid. MS (m/z): [M+H]+ 410.9.

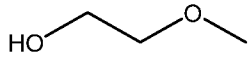
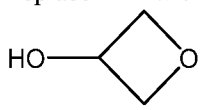
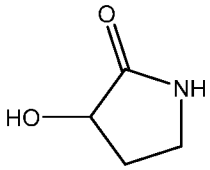
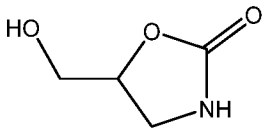
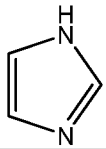
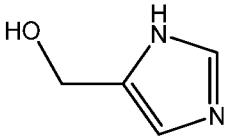
[00457] Step 3: Synthesis of 5-((2-hydroxyethoxy)methyl)-6-iodo-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**I-29**): In a 10 mL flame-dried-microwave-vial was added sodium hydride (60% in mineral oil) (7.1 mg, 0.49 mmol) in dry DMF (0.7 mL). Then, ethylene glycol (**I-28**, 25.1 µL, 0.45 mmol) was added. The mixture was stirred at r.t. for 5 min and compound **I-27** (80.0 mg, 0.20 mmol) in DMF (0.7 mL) was added dropwise. The reaction was stirred at r.t. for 18 h then quenched with ammonium chloride. The organic layers were separated and the aqueous layer was extracted (2x) with EtOAc. The organic layers were combined, washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to provide a brownish oil. This crude material was recrystallized from DCM/diethyl ether, filtered and washed with diethyl ether (3x) to afford compound **I-29** as a yellow solid. MS (m/z): $[M+H]^+$ 437.0.

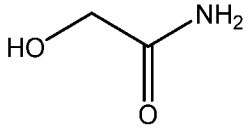
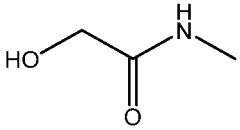
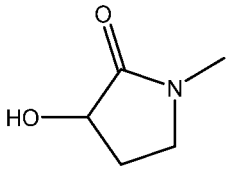
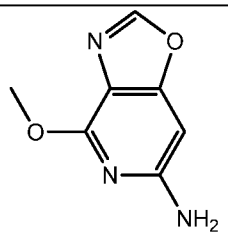
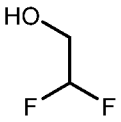
[00458] Step 4: Synthesis of 5-((2-hydroxyethoxy)methyl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-2-carbonitrile (**C1248**): In a 10 mL flame-dried-microwave-vial were successively added compound **I-29** (50.0 mg, 0.12 mmol), 4-methoxybenzo[d]oxazole (**I-15**, 26.6 mg, 0.17 mmol), lithium *tert*-butoxide (47.3 mg, 0.57 mmol) and palladium(II) acetate (2.63 mg, 10 mol %) in dry DMF (0.40 mL). Then, the reaction mixture was degassed with argon and heated at 95 °C for 12 h. The reaction was cooled to r.t. and poured in a separation funnel containing ammonium chloride and EtOAc. The organic layers was separated and the aqueous layer was extracted (2x) with EtOAc. The organic layers were combined, washed with brine, dried over sodium sulfate, filtered and concentrated in vacuum. This crude product was purified by flash column chromatography (40 g, SiO_2 column_gradient 0 to 10% MeOH in DCM) to afford the title product. ^1H NMR (500 MHz, DMSO): δ 8.08 (dd, J = 8.3, 1.1 Hz, 2H), 7.53 – 7.46 (m, 3H), 7.33 – 7.28 (m, 1H), 7.27 (dd, J = 6.6, 2.7 Hz, 2H), 6.92 – 6.87 (m, 1H), 4.63 (s, 1H), 4.00 (s, 3H), 3.31 – 3.26 (m, 2H), 3.20 (t, J = 5.4 Hz, 2H). MS (m/z): $[M+H]^+$ 458.0; purity > 97%.

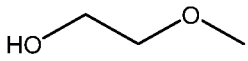
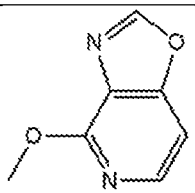
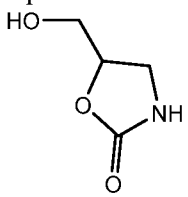
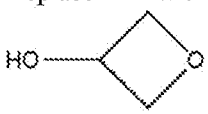
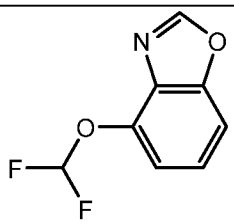
[00459] Table 12 below provides additional compounds that can be synthesized similarly to the methods described in the above steps 1-4, optionally substituting the listed compound for **I-15**, and/or substituting for **I-24** and/or **I-28** where indicated**.** Data for compounds synthesized is provided in columns 3-5.

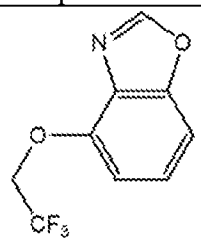
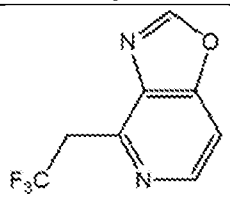
Table 12

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1056	Replace **I-24** with **I-1** Replace **I-28** with CH_3OH	(400 MHz, DMSO) δ 12.69 (s, 1H), 7.56 (d, *J* = 6.2 Hz, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.32 – 7.19 (m, 3H), 6.88 – 6.82 (m, 1H), 4.45 (s, 2H), 3.95 (s, 3H), 3.01 (s, 3H).	99.6	471.2
C1103	Replace **I-24** with **I-1** Replace **I-28** with H_2O	(500 MHz, DMSO) δ 7.61 (d, J = 7.5 Hz, 2H), 7.45 (t, J = 7.8 Hz, 2H), 7.28-7.24 (m,3H), 6.90 (d, J = 6.9 Hz, 1H), 5.21 (t, J = 5.0 Hz, 1H), 4.57 (d, J = 5.2 Hz, 2H), 3.99 (s, 3H).	99.3	456.9
C1109	Replace **I-24** with **I-1** Replace **I-28** with $NH(CH_3)_2$	(500 MHz, CD3CN) δ 7.65 (d, J = 7.5 Hz, 2H), 7.46 (t, J = 7.7 Hz, 2H), 7.38 – 7.34 (m, 1H), 7.33 – 7.26 (m, 2H), 6.92 (dd, J = 7.5, 1.1 Hz, 1H), 4.33 (s, 2H), 4.03 (s, 3H), 2.91 (s, 6H)	99.0	484.2
C1136	Replace **I-24** with **I-1** Replace **I-28** with CH_3SH	(500 MHz, DMSO) δ 7.62 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.34 – 7.21 (m, 3H), 6.89 (d, J = 7.4 Hz, 1H), 4.01 (s, 3H), 3.92 (s, 2H), 1.95 (s, 3H).	99.0	487.1
C1139	Replace **I-28** with CH_3OH	(500 MHz, DMSO) δ 8.08 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.8 Hz, 2H), 7.34 – 7.25 (m, 3H), 6.94 – 6.87 (m, 1H), 4.56 (s, 2H), 4.00 (s, 3H), 3.10 (s, 3H).	95.6	428.2
C1145	 Replace **I-28** with CH_3OH	(500 MHz, DMSO) δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.52 – 7.46 (m, 3H), 7.32 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 1.7 Hz, 1H), 4.55 (s, 2H), 4.01 (s, 3H), 3.09 (s, 3H).	97.3	462.0
C1146	Replace **I-24** with **I-1** Replace **I-28** with 	(400 MHz, DMSO) δ 7.59 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 5.4 Hz, 1H), 7.39 (t, J = 7.6 Hz, 2H), 7.27 – 7.21 (m, 3H), 6.85 (d, J = 7.6 Hz, 1H), 5.31 (s, 2H), 3.97 (s, 3H), 3.91 (d, J = 6.2 Hz, 2H).	96.2	515.1

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1151	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 7.62 (d, J = 7.4 Hz, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.32 – 7.23 (m, 3H), 6.89 (dd, J = 6.3, 2.8 Hz, 1H), 4.54 (s, 2H), 4.00 (s, 3H), 3.09 (dd, J = 5.6, 4.3 Hz, 2H), 2.99 (s, 3H).	100	515.2
C1152	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 7.60 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.33 – 7.25 (m, 3H), 6.90 (dd, J = 6.7, 2.3 Hz, 1H), 4.54 (s, 2H), 4.46 (p, J = 5.7 Hz, 1H), 4.36 (t, J = 6.8 Hz, 2H), 4.10 (dd, J = 7.0, 5.7 Hz, 2H), 4.00 (s, 3H).	99.7	513.1
C1159	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 7.64 (d, J = 7.4 Hz, 2H), 7.62 (s, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.33 – 7.25 (m, 3H), 6.90 (dd, J = 6.6, 2.4 Hz, 1H), 4.80 (dd, J = 43.7, 12.0 Hz, 2H), 4.00 (s, 3H), 3.83 – 3.78 (m, 1H), 2.92 – 2.86 (m, 2H), 1.84 – 1.76 (m, 1H), 1.41 (m, 1H).	99.1	540.2
C1177	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 8.27 (s, 1H), 7.68 (d, J = 7.5 Hz, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.33 – 7.22 (m, 3H), 6.90 (dd, J = 7.7, 1.2 Hz, 1H), 5.01 (t, J = 5.8 Hz,1H), 4.66-4.51 (m, 2H), 4.40 (dd, J = 9.1, 6.5 Hz, 1H), 4.0 (s, 3H), 3.75 (t, J = 8.6 Hz,1H), 3.45 – 3.38 (m, 2H).	99.9	556.3
C1180	Replace **I-24** with **I-1** Replace **I-28** with 	(400 MHz, DMSO) δ 7.63 – 7.53 (m, 3H), 7.37 (t, J = 7.4 Hz, 2H), 7.31 – 7.22 (m, 3H), 7.11 (s, 1H), 6.92 (d, J = 6.4 Hz, 1H), 6.81 (s, 1H), 5.38 (s, 2H), 4.02 (s, 3H).	99.0	507.0
C1182	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, CD_3CN) δ 7.64 (d, J = 7.9 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 7.31 – 7.18 (m, 3H), 7.03 (s, 1H), 6.88 (d, J = 8.0 Hz, 1H), 6.70 (s, 1H), 4.69 (s, 2H), 4.36 (s, 2H), 4.01 (s, 3H).	97.9	537.0

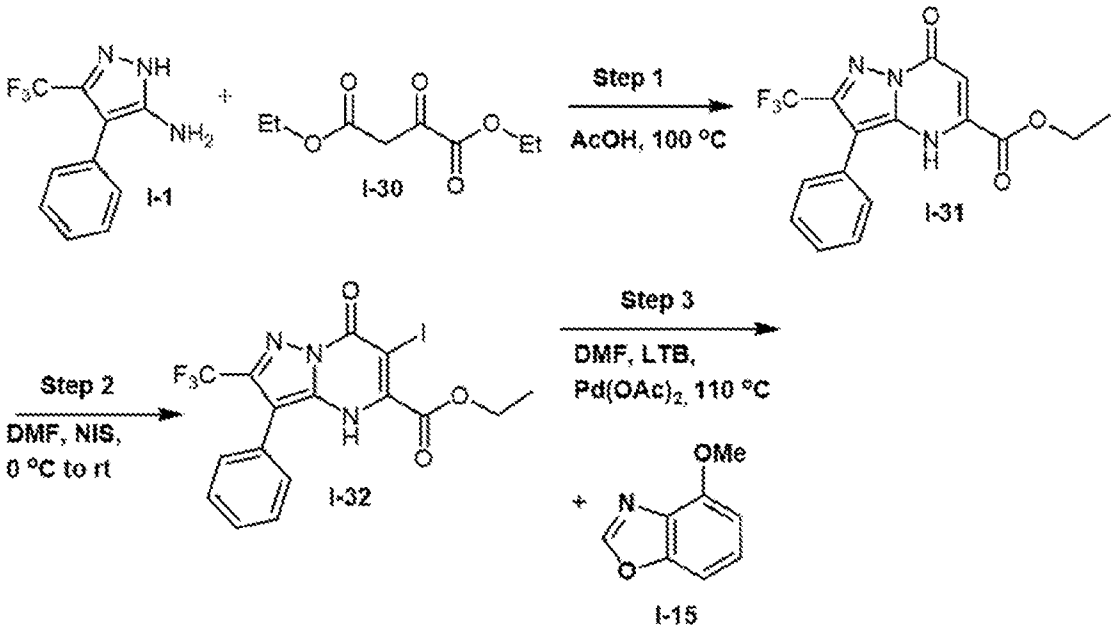
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1198	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 7.72 (s, 1H), 7.56 (d, J = 7.5 Hz, 2H), 7.41 (t, J = 7.7 Hz, 2H), 7.30-7.25 (m, 2H), 6.90 (t, J = 7.1 Hz, 1H), 6.69-6.66 (m, 2H), 4.93 (s, 2H), 4.39 (s, 2H), 3.71 (s, 3H).	98.95	514.0
C1199	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 8.97 (s, 1H), 7.57 (d, J = 7.2 Hz, 2H), 7.43-7.40 (m, 2H), 7.31-7.28 (m, 1H), 6.93 (t, J = 8.3 Hz, 1H), 6.75-6.69 (m, 2H), 4.96 (s, 2H), 4.48 (s, 2H), 3.72 (s, 3H), 2.75 (d, J = 4.6 Hz, 3H).	98.54	528.1
C1225	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 7.63 (d, J = 7.4 Hz, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.32 – 7.24 (m, 3H), 6.89 (dd, J = 6.1, 2.9 Hz, 1H), 4.79 (q, J = 12.0 Hz, 2H), 4.00 (s, 3H), 3.90 – 3.86 (m, 1H), 3.01 – 2.94 (m, 2H), 2.57 (s, 3H), 1.83-1.76 (m, 1H), 1.38-1.34 (m, 1H).	97.8	554.3
C1226	Replace **I-24** with **I-1**	(500 MHz, DMSO) δ 7.60 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.36 – 7.26 (m, 3H), 6.92 – 6.89 (m, 1H), 4.59 (s 2H), 4.00 (s, 3H), 3.28 – 3.25 (m, 2H), 3.21 – 3.17 (m, 2H).	98.3	501.2
C1227	 Replace **I-28** with CH_3OH	(400 MHz, DMSO) δ 8.07 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.8 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 6.21 (s, 1H), 5.86 (s, 2H), 4.47 (s, 2H), 3.94 (s, 3H), 3.11 (s, 3H).	99.7	444.2
C1232	Replace **I-24** with **I-1** Replace **I-28** with 	(500 MHz, DMSO) δ 7.57 (d, J = 6.7 Hz, 2H), 7.47 (t, J = 7.3 Hz, 2H), 7.42 – 7.28 (m, 3H), 6.95 – 6.90 (m, 1H), 5.92 (tt, J = 54.8, 3.5 Hz, 1H), 4.75 (s, 2H), 4.00 (s, 3H), 3.65 (td, J = 15.1, 3.7 Hz, 2H).	99.8	521.2

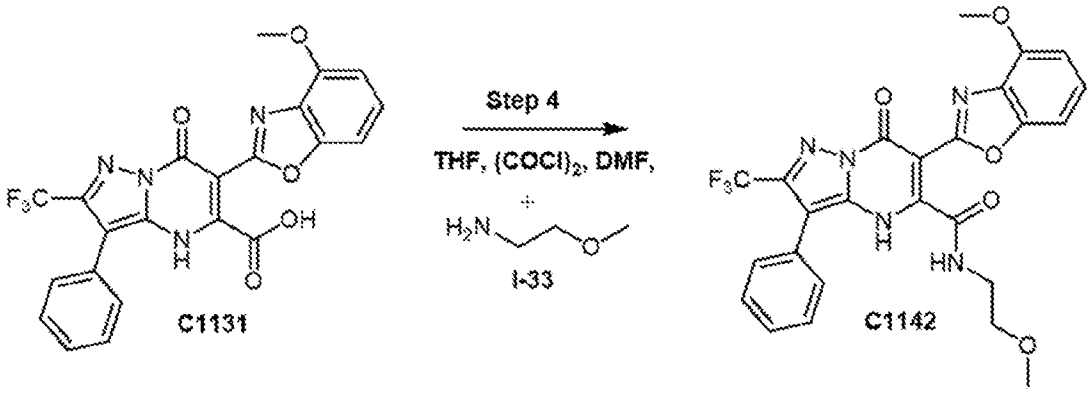
Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1243	Replace **I-28** with 	(500 MHz, DMSO): δ 8.11 – 8.06 (m, 2H), 7.50 – 7.45 (m, 2H), 7.32 – 7.28 (m, 1H), 7.28 – 7.26 (m, 2H), 7.07 (s, 1H), 6.92 – 6.88 (m, 1H), 4.62 (s, 2H), 4.00 (s, 3H), 3.40 – 3.37 (m, 2H), 3.14 (dd, *J* = 5.6, 4.3 Hz, 2H), 3.02 (s, 3H).	99	471.2
C1246	 Replace **I-28** with CH_3OH	(500 MHz, DMSO) δ 8.09 – 8.02 (m, 3H), 7.52 – 7.46 (m, 2H), 7.44 (d, J = 5.7 Hz, 1H), 7.33-7.30 (m, 1H), 4.56 (s, 2H), 4.06 (s, 3H), 3.08 (s, 3H).	99.6	429.1
C1251	Replace **I-28** with 	(500 MHz, DMSO): δ 8.09 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.51 – 7.44 (m, 2H), 7.33 – 7.24 (m, 3H), 6.91 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.08 (t, *J* = 5.7 Hz, 1H), 4.70 (d, *J* = 17.6 Hz, 1H), 4.58 (d, *J* = 17.6 Hz, 1H), 4.54 – 4.47 (m, 1H), 4.01 (s, 3H), 3.78 (t, *J* = 8.7 Hz, 1H), 3.53 (td, *J* = 5.6, 2.2 Hz, 2H), 3.44 (dd, *J* = 8.3, 6.7 Hz, 1H).	99	513.2
C1259	Replace **I-28** with 	(500 MHz, DMSO): δ 8.05 (d, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.34 – 7.26 (m, 3H), 6.94 – 6.89 (m, 1H), 4.61 (s, 2H), 4.55 – 4.49 (m, 1H), 4.41 (t, *J* = 6.8 Hz, 2H), 4.14 (dd, *J* = 7.1, 5.7 Hz, 2H), 4.00 (s, 3H).	99	470.2
C1261	 Replace **I-28** with CH_3OH			

Compound ID	Compound **I-15** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1262	 Replace **I-28** with CH_3OH			
C1263	 Replace **I-28** with 			

Example 12

[00460] Synthesis of 6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxylic acid (**C1131**) and 6-(4-methoxybenzo[d]oxazol-2-yl)-*N*-(2-methoxyethyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1142**) were carried out in three and four steps, respectively, as follows:





[00461] Step 1: Synthesis of ethyl 7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylate (**I-31**): To a stirred solution of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine (**I-1**, 1.0 g, 4.48 mmol) in AcOH (5 mL) was added diethyl oxalacetate (**I-30**, 0.98 g, 5.2 mmol). The reaction mixture was heated at 100 °C for 120 min. The acetic acid was removed *in vacuo*. Et_2O/Hex 1:1 (5 mL) was added and stirred at r.t. for 5 min. The mixture was filtered, washed with Et_2O/Hex 1:1 (2x30 mL) and dried *in vacuo* to afford the compound **I-31** as a white solid. MS (m/z): 352.1 $[M+1]^+$, 100%.

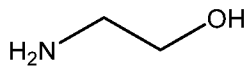
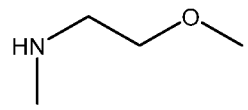
[00462] Step 2: Synthesis of ethyl 6-iodo-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-a]pyrimidine-5-carboxylate (**I-32**): To a stirred solution of compound **I-31** (1.2 g, 3.36 mmol) in DMF (11.2 mL) cooled at 0 °C (white suspension) was added *N*-iodosuccinimide (0.87 g, 3.52 mmol), then warmed to r.t. After 1 h, LCMS showed complete conversion. The reaction mixture was poured onto dil $Na_2S_2O_3$ (30 mL). The precipitated solid was filtered, washed with dil $NaHCO_3$ and dried *in vacuo* to give compound **I-32** as a white solid. MS (m/z): 477.9 $[M+1]^+$.

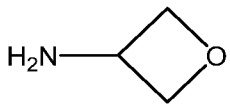
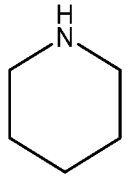
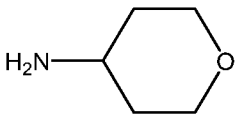
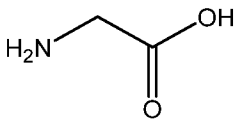
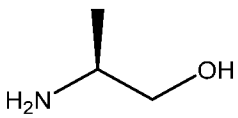
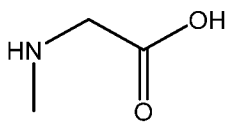
[00463] Step 3: Synthesis of 6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxylic acid (**C1131**): Compound **I-32** (300 mg, 629 µmol), 4-methoxybenzo[d]oxazole (**I-15**, 1.5 eq, 141 mg, 943 µmol), Lithium *tert*-butoxide (292 µL, 3.14 mmol), palladium(II) acetate (14.3 mg, 62.9 µmol) were added in DMF (2 mL). The reaction was degassed with nitrogen then heated at 110 °C for 4 h. The reaction was cooled to r.t. and the product was crashed out with 1N HCl and then filtered. The solid obtained was purified by reverse phase chromatography 0 – 100% MeCN/H_2O (0.1% ammonium bicarbonate buffer) and lyophilized to give compound **C1131** as a white solid. ^1H NMR (500 MHz, DMSO) δ 7.60 (d, J = 7.6 Hz, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 7.24 – 7.21 (m, 2H), 6.89 – 6.84 (m, 1H), 3.98 (s, 3H); MS (m/z): 471.1/427.1 $[M+1]^+$, 100%.

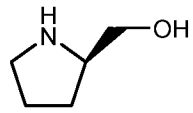
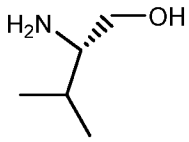
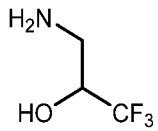
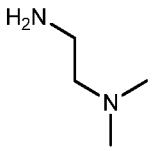
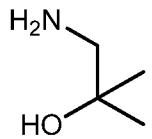
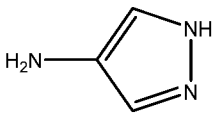
[00464] Step 4: Synthesis of 6-(4-methoxybenzo[d]oxazol-2-yl)-*N*-(2-methoxyethyl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxamide (**C1142**): A solution of compound **C1131** (25.0 mg, 53.2 µmol) in THF (500 µL) was cooled to 0 °C. oxalyl chloride (13.8 µL, 159 µmol) was added followed by one drop of DMF and the reaction was stirred for 0.5h. The reaction mixture was concentrated, THF (500 µL) was added and concentrated again. THF (500 µL) was added and the mixture cooled to 0 °C. 2-Methoxyethylamine (**I-33**, 5.60 µL, 79.7 µmol) was added and the reaction was stirred overnight. The volatiles were removed *in vacuo* and the residue purified by reverse phase chromatography 0 – 100% MeCN/H_2O (0.1% ammonium bicarbonate buffer) and lyophilized to give compound **C1142**. ^{1}H NMR (500 MHz, DMSO) δ 8.25 (t, *J* = 5.8 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.29 – 7.21 (m, 2H), 6.90 (dd, *J* = 7.8, 1.2 Hz, 1H), 3.99 (s, 3H), 3.37 (t, *J* = 6.0 Hz, 2H), 3.28 – 3.24 (m, 2H), 3.24 (s, 3H); MS (m/z): 527.9 $[M+1]^+$, 96%.

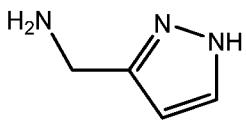
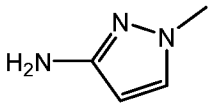
[00465] Table 13 below provides additional compounds that can be synthesized similarly to the methods described in the above steps 1-4, substituting the listed compound for **I-33**, or substituting **I-24** for **I-1** where indicated. Data for compounds synthesized is provided in columns 3-5.

Table 13

Compound ID	Compound **I-33** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1132	NH_3	(500 MHz, DMSO) δ 7.61 (d, *J* = 7.5 Hz, 2H), 7.55 (br s, 1H), 7.40 – 7.35 (m, 2H), 7.27 – 7.21 (m, 2H), 7.17 – 7.16 (m, 1H), 6.98 (br s, 2H), 6.81 (dd, *J* = 7.5, 1.6 Hz, 1H), 3.91 (s, 3H)	100	470.0
C1178		(500 MHz, DMSO) δ 8.22 (t, *J* = 5.5 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.24 (dt, *J* = 8.1, 7.5 Hz, 2H), 6.89 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.67 (t, *J* = 5.4 Hz, 1H), 3.98 (s, 3H), 3.41 (q, *J* = 6.0 Hz, 2H), 3.17 (q, *J* = 6.2 Hz, 2H).	96.0	513.13
C1179		(500 MHz, DMSO) (mixture of rotamers): δ 7.56 (d, *J* = 7.5 Hz, 2H), 7.46 – 7.41 (m, 2H), 7.34 – 7.29 (m, 1H), 7.23 (dd, *J* = 13.3, 7.4 Hz, 1H), 6.91 – 6.84 (m, 1H), 4.03 (s, 1.34H), 3.98 (s, 1.66H), 3.58 – 3.51 (m, 2H), 3.49 – 3.43 (m, 2H), 3.23 (s, 1.80H), 3.15 (s, 1.20H), 2.95 (s, 1.66H), 2.92 (s, 1.30H).	98.03	541.16

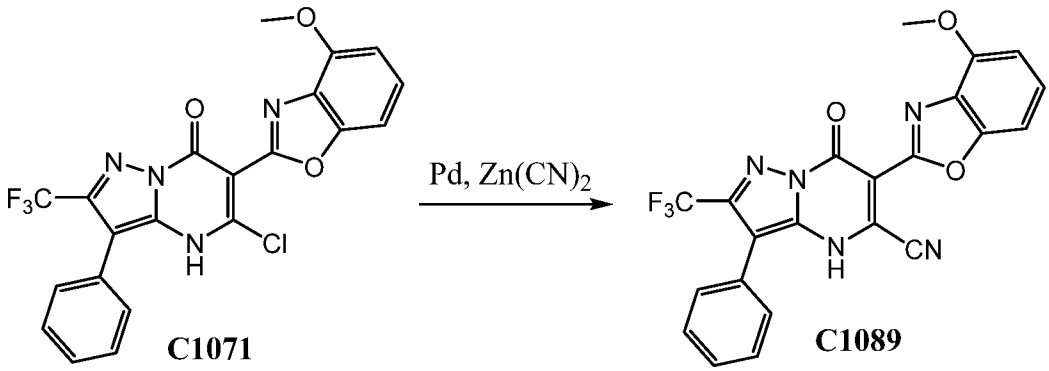
Compound ID	Compound **I-33** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1185		(500 MHz, DMSO) δ 8.90 (d, *J* = 6.7 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.48 – 7.42 (m, 2H), 7.34 – 7.30 (m, 1H), 7.24 (d, *J* = 7.1 Hz, 2H), 6.88 (dd, *J* = 7.1, 1.9 Hz, 1H), 4.82 – 4.75 (m, 1H), 4.67 – 4.62 (m, 2H), 4.53 (t, *J* = 6.5 Hz, 2H), 3.96 (s, 3H).	95.7	525.13
C1186		(500 MHz, DMSO) δ 7.55 (d, *J* = 7.5 Hz, 2H), 7.45 (dd, *J* = 10.6, 4.9 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.28 – 7.22 (m, 2H), 6.92 – 6.85 (m, 1H), 3.99 (s, 3H), 3.53 – 3.41 (m, 4H), 1.62 – 1.46 (m, *J* = 24.3 Hz, 6H).	98.2	537.16
C1194		(500 MHz, DMSO) δ 8.41 – 8.33 (m, 1H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.40 – 7.36 (m, 1H), 7.31 – 7.24 (m, 2H), 6.93 – 6.89 (m, 1H), 3.97 (s, 3H), 3.77 – 3.71 (m, 3H), 3.30 (td, *J* = 11.4, 2.1 Hz, 3H), 1.71 – 1.63 (m, 2H), 1.42 – 1.33 (m, 2H).	99	553.16
C1195		(500 MHz, MeOD) δ 7.66 (d, *J* = 7.4 Hz, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 8.2 Hz, 1H), 7.27 – 7.17 (m, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 4.03 (s, 3H), 4.00 (s, 2H).	96.3	527.11
C1196		(500 MHz, DMSO) δ 8.17 – 8.06 (m, 1H), 7.66 – 7.60 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.31 – 7.21 (m, 2H), 6.90 (d, *J* = 8.6 Hz, 1H), 3.98 (s, 3H), 3.72 (dt, *J* = 12.8, 6.4 Hz, 1H), 3.24 (dd, *J* = 10.6, 6.2 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 3H).	99	527.14
C1197		(500 MHz, DMSO) mixture of rotamers δ 12.63 (s, 1H), 7.60 – 7.52 (m, 2H), 7.44 (dd, *J* = 16.3, 7.9 Hz, 2H), 7.33 (dt, *J* = 11.2, 7.4 Hz, 1H), 7.29 – 7.19 (m, 2H), 6.87 (d, *J* = 7.4 Hz, 1H), 4.11 (s, 0.92H), 4.07 (s, 1.14 H), 4.06 – 3.98 (m, 3H), 2.99 (s, 1.74H), 2.96 (s, 1.43H).	99	541.12

Compound ID	Compound **I-33** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1207		(500 MHz, DMSO): δ 7.54 (dd, *J* = 12.3, 7.5 Hz, 2H), 7.46 (dd, *J* = 15.2, 7.6 Hz, 2H), 7.35 (dd, *J* = 15.9, 8.2 Hz, 1H), 7.31 – 7.22 (m, 2H), 6.90 (t, *J* = 7.3 Hz, 1H), 3.98 (s, 3H), 3.95 – 3.89 (m, 1H), 3.64 (dd, *J* = 10.6, 4.1 Hz, 1H), 3.56 – 3.52 (m, 2H), 3.24 (ddd, *J* = 8.9, 8.4, 2.7 Hz, 1H), 1.98 – 1.79 (m, 4H).	95.1	553.2
C1208		(500 MHz, DMSO) δ 8.13 (d, *J* = 9.4 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 2H), 7.45 (dd, *J* = 10.6, 4.8 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 8.1 Hz, 1H), 7.26 – 7.20 (m, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 3.98 (s, 3H), 3.54 – 3.48 (m, 1H), 3.43 (dd, *J* = 11.0, 4.9 Hz, 1H), 3.34 (dd, *J* = 10.9, 5.7 Hz, 1H), 1.94 – 1.82 (m, 1H), 0.81 (dd, *J* = 6.8, 3.0 Hz, 6H).	97.9	555.17
C1209		(500 MHz, DMSO): δ 8.47 (d, *J* = 5.8 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.49 – 7.43 (m, 2H), 7.37 – 7.32 (m, 1H), 7.30 – 7.21 (m, 2H), 6.90 (dd, *J* = 7.9, 1.1 Hz, 1H), 4.17 – 4.10 (m, 1H), 3.97 (s, 3H), 3.50 (ddd, *J* = 13.6, 6.6, 4.3 Hz, 1H), 3.20 (ddd, *J* = 14.3, 8.2, 5.9 Hz, 1H).	95.4	581.1
C1212		(500 MHz, DMSO) δ 8.27 (t, *J* = 5.6 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.28 – 7.21 (m, 2H), 6.89 (d, *J* = 7.2 Hz, 1H), 3.98 (s, 3H), 3.19 (dd, *J* = 12.3, 6.3 Hz, 2H), 2.37 (t, *J* = 6.3 Hz, 2H), 2.18 (s, 6H).	99	540.2
C1219		(500 MHz, DMSO) δ 8.28 – 8.20 (m, 1H), 7.68 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.27 (t, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 6.90 (dd, *J* = 8.1, 0.8 Hz, 1H), 3.98 (s, 3H), 3.05 (d, *J* = 6.1 Hz, 2H), 1.04 (s, 6H).	98.14	541.2
C1244		(500MHz, DMSO) δ 10.21 (s, 1H), 7.64 – 7.59 (m, 4H), 7.43 – 7.37 (m, 3H), 7.30 – 7.24 (m, 1H), 7.21 – 7.17 (m, 2H), 6.83 – 6.79 (m, 1H), 3.92 (s, 1H), 3.86 (s, 3H).	97.2	536.3

Compound ID	Compound **I-33** replacement	^{1}H NMR	Purity (%)	MS (m/z)
C1245		(500 MHz, DMSO) δ 8.60 (s, 1H), 7.68 – 7.63 (m, 2H), 7.53 (s, 1H), 7.32 – 7.19 (m, 3H), 7.16 (s, 1H), 7.06 (s, 1H), 6.96 (s, 1H), 6.89 – 6.86 (m, 1H), 6.19 – 6.17 (m, 1H), 4.32 – 4.26 (m, 2H), 3.97 (s, 3H).	95.2	550.2
C1249	Replace **I-1** with **I-24** Isolate after Step 3	(500 MHz, DMSO) δ 8.09 (d, *J* = 7.3 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.30 – 7.18 (m, 3H), 6.86 (dd, *J* = 7.0, 2.0 Hz, 1H), 3.98 (s, 3H).		428.0
C1256		(500 MHz, DMSO) δ 10.31 (s, 1H), 8.38 (s, 2H), 7.67 – 7.65 (m, 2H), 7.52 – 7.50 (m, 1H), 7.48 – 7.44 (m, 2H), 7.35 – 7.31 (m, 1H), 7.22 – 7.20 (m, 1H), 6.88 – 6.85 (m, 1H), 6.32 – 6.30 (m, 1H), 3.93 (s, 3H), 3.71 (s, 3H)	95	550.2

Example 13

[00466] Synthesis of 6-(4-methoxybenzo[*d*]oxazol-2-yl)-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carbonitrile (**C1089**) was carried out in one step as follows:

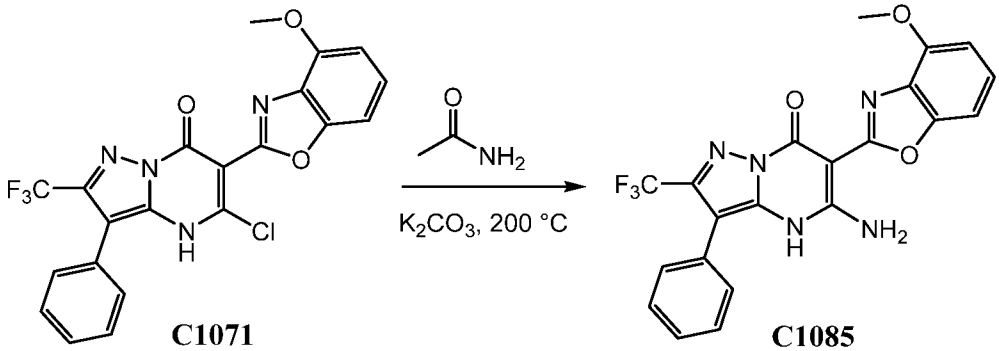


[00467] **Step 1**: Compound **C1071** (see Example 7, Step 2, 20.0 mg, 0.0434 mmol), $Pd(TFA)_2$ (1.44 mg, 0.00434 mmol), Zinc cyanide (5.20 mg, 0.0434 mmol), TrixPhos (3.53 mg, 0.00868 mmol), Zn (0.203 μL, 0.0217 mmol) were charged successively to a glass tube equipped with a magnetic stir bar and Teflon screw-cap. The tube was evacuated and back-filled with nitrogen. DMAC (anhydrous, 99.8%, 3 mL) was added via syringe and the resulting reaction mixture was degassed. The reaction mixture was then heated at 110 °C for 14 hours. The reaction mixture was then cooled to room temperature, diluted with MeCN, filtered through Celite. The solvent was evaporated and the crude material was purified by semi-prep HPLC-MS using MeCN and 10 mM aqueous AmForm buffer as eluent to afford compound **C1089** (8.00 mg, 41 %). **^{1}H NMR** (500 MHz, DMSO) δ 8.27 (s, 1H), 7.57 (d, J =

7.3 Hz, 2H), 7.48 (t, J = 7.7 Hz, 2H), 7.37 - 7.32 (m, 3H), 6.94 (dd, J = 7.3, 1.7 Hz, 1H), 4.04 (s, 3H). **LCMS** m/z: $[M+H]^+$ = 452.2; 5-100% MeCN/H_2O (0.1% AMF buffer) over 7 min.

Example 14

[00468] Synthesis of 5-amino-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1085**) was carried out in one step as follows:

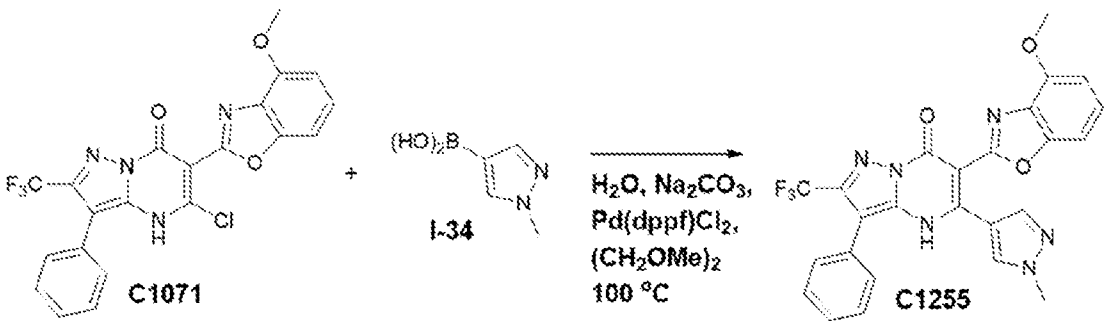


C1071 **C1085**

[00469] Step 1: A mixture of acetamide (51.8 mg, 868 µmol), C1071 (see Example 7, Step 2, 10.0 mg, 21.7 µmol), and K_2CO_3 (51.8 mg, 109 µmol) was heated at 200 °C for 2 h. The reaction mixture was dissolved in 1 mL DMSO and purified by reverse flash chromatography (KP-C18-H5 reverse phase column using MeCN and 10 mM aqueous AmForm buffer as eluent) to afford C1085 (2 mg, 21 %). ^{1}**H NMR** (500 MHz, DMSO) δ 8.15 (s, 1H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.27 – 7.19 (m, 2H), 7.15 (d, *J* = 8.1 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 3.96 (s, 3H). **LCMS** m/z: $[M+H]^+$ = 442.0; 5-100% MeCN/H_2O (0.1% AMF buffer) over 7 min.

Example 15

[00470] Synthesis of 6-(4-methoxybenzo[d]oxazol-2-yl)-5-(1-methyl-1*H*-pyrazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1255**) was carried out in one step as follows:

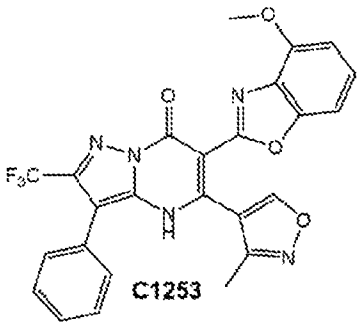


C1071 **C1255**

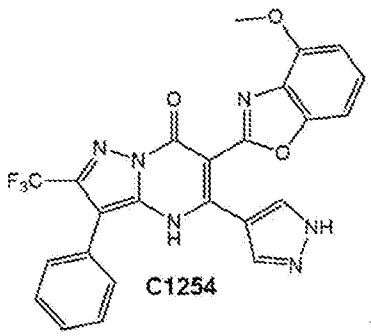
[00471] Step 1: A mixture of compound **C1071** (see Example 7, Step 2, 30.0 mg, 62.9 µmol, see Example 7), (1-methyl-1H-pyrazol-4-yl)boronic acid (**I-34**, 12.5 mg, 94.4 µmol), sodium

carbonate (13.3 mg, 126 μmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(ll) (30.6 mg, 37.4 μmol) in water (110 μL) and dimethoxyethane (220 μL)was degassed by bubbling under nitrogen for 5 min. The reaction was stirred overnight at 110 °C. The crude mixture was concentrated *in vacuo*, then purified via reverse phase chromatography (KP-C18-H5, using a gradient 0 to 100% MeCN in 10 mM aqueous AmForm buffer) to afford compound **C1255** after lyophilization. ^{1}H NMR (500 MHz, DMSO-d6) δ 7.94 (s, 1H), 7.56 (d, *J* = 7.3 Hz, 2H), 7.53 – 7.46 (m, 2H), 7.45 – 7.35 (m, 2H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.05 (s, 1H), 6.98 (d, *J* = 7.7 Hz, 1H), 3.98 (s, 3H), 3.76 (s, 3H); MS (m/z): 507.3 $[M+1]^+$.

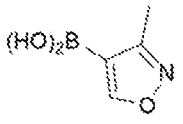
[00472] Compounds 6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-(3-methylisoxazol-4-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1253**) and 6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-5-(1*H*-pyrazol-4-yl)-2-(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-7(4*H*)-one (**C1254**)


C1253

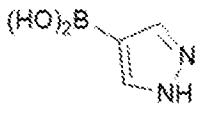
and


C1254

were prepared similarly to the above method, replacing **I-34** with



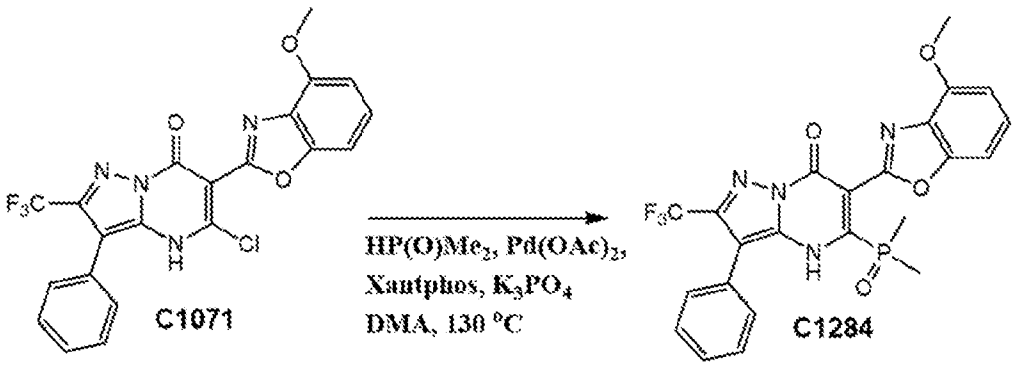
and



, respectively.

Example 16

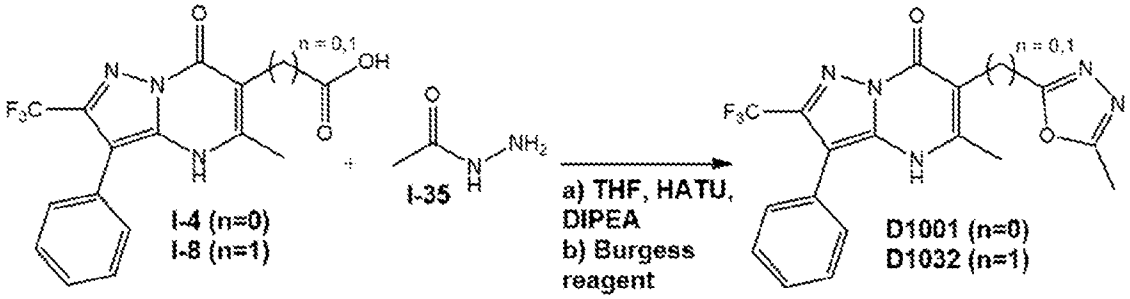
[00473] Synthesis of 5-(dimethylphosphoryl)-6-(4-methoxybenzo[*d*]oxazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**C1284**) was carried out in one step as follows:



[00474] Step 1: A mixture of compound **C1071** (see Example 7, Step 2, 20.0 mg, 0.043 mmol), dimethylphosphine oxide (10.0 mg, 0.130 mmol), $Pd(OAc)_2$ (1.48 mg, 0.00651 mmol), Xantphos (7.69 mg, 0.013 mmol), and K_3PO_4 (27.6 mg, 0.130 mmol) in DMF (500 µL) was degassed with N_2. The reaction mixture was then heated at 130 °C for 3 h after which it was filtered over celite and washed with MeOH. The filtrate was evaporated *in vacuo* and the resulting material was purified by reverse phase HPLC (AmF/MeCN) to afford Compound **C1284**. ^{1}H NMR (500 MHz, DMSO) δ 7.69 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.32 – 7.23 (m, 3H), 6.89 (d, J = 7.4 Hz, 1H), 4.00 (s, 3H), 1.69 (s, 3H), 1.67 (s, 3H); MS (m/z): 503.1 $[M+1]^+$, 100%.

Example 17

[00475] Synthesis of 5-methyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1001**) or 5-methyl-6-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1032**) was carried out in one step as follows:

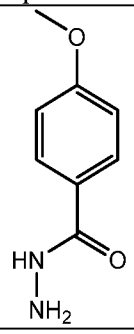
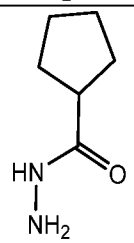
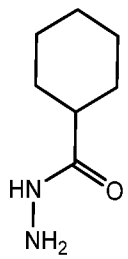
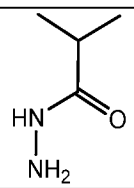


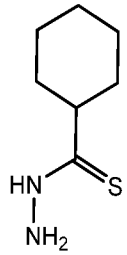
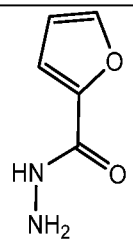
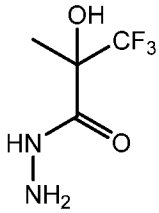
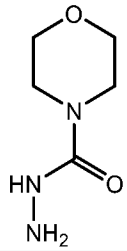
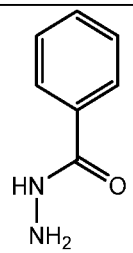
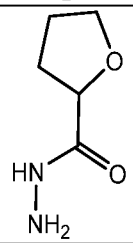
[00476] Step 1: Preparation of 5-methyl-6-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1032**): To a stirred suspension of 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetic acid (**I-8**, 70 mg, 0.2 mmol, see Example 2) in THF (2 mL) was added HATU (76 mg, 0.2 mmol), acetylhydrazine (**I-35**, 15 mg, 0.2 mmol) and DIPEA (70 µL, 0.40 mmol). The reaction mixture was stirred at r.t. for 18h. After addition of Burgess reagent (124 mg, 0.50 mmol), the reaction mixture was stirred at r.t. for 2 days. More Burgess reagent (124 mg, 0.50 mmol) was added and the reaction mixture was heated at 40 °C for 3h and concentrated. The residue was purified by reverse flash chromatography (KP-C18-H5, using a gradient 0 to 100% MeCN in 10 mM aqueous ammonium formate buffer) to afford compound **D1032** (122 mg, 0.27 mmol, 75%) as a white solid after lyophilization. ^{1}H NMR (500 MHz, DMSO) δ 12.36 (s, 1H), 7.53 – 7.42 (m, 5H), 4.11 (s, 2H), 2.44 (s, 3H), 2.41 (s, 3H); MS (m/z): 390.0 $[M+1]^+$, 99.9%.

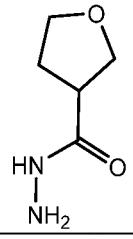
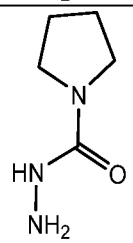
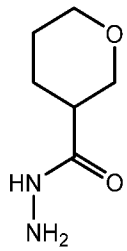
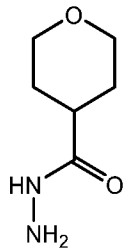
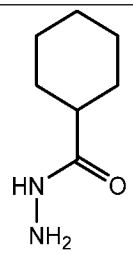
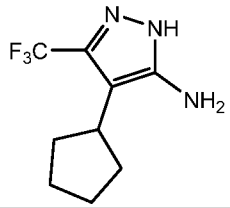
[00477] **Step 1**: 5-methyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**D1001**) was prepared following this method starting from compound **I-4** (see Example 1). ^{1}H NMR (500MHz, DMSO) δ 7.54 (d, *J* = 7.4 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 2.55 (s, 3H), 2.31 (s, 3H); MS (m/z): 376.1 $[M+1]^+$, 99.0%.

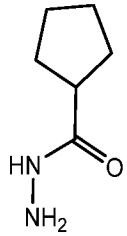
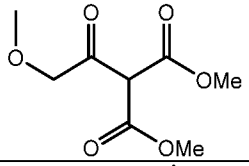
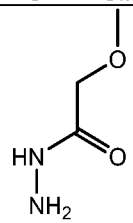
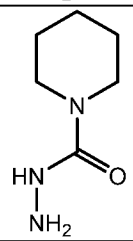
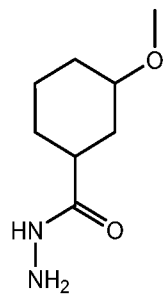
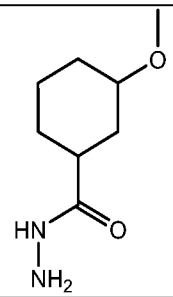
[00478] Table 14 below provides additional compounds that can be synthesized similarly to the methods described in the above step from **I-4** unless indicated otherwise by substituting the listed compound for **I-35**, and/or replacing **I-1** and/or **I-2** where indicated to provide the suitable analog of **I-4** (per Example 1). Data for compounds synthesized is provided in columns 3-5.

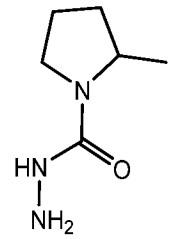
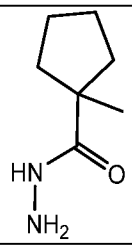
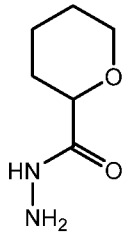
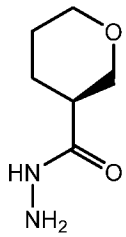
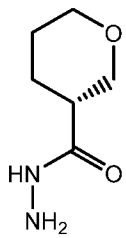
Table 14

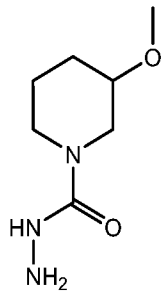
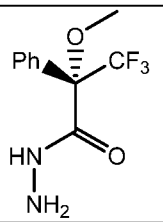
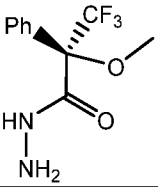
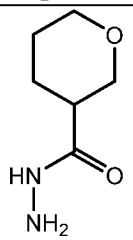
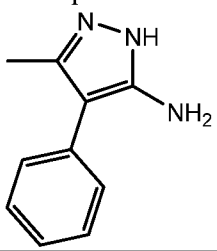
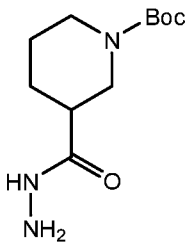
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1002		(500MHz, DMSO) δ 13.05 (s, 1H), 7.98 (d, *J* = 8.6 Hz, 2H), 7.55 – 7.42 (m, 5H), 7.18 (d, *J* = 8.7 Hz, 2H), 3.87 (s, 3H), 2.48 (s, 3H).	97.3	468.1
D1003		(500MHz, DMSO) δ 7.55 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 3.43-3.36 (m, 1H), 2.29 (s, 3H), 2.12 – 2.04 (m, 2H), 1.90-1.83 (m, 2H), 1.78 – 1.62 (m, 4H).	97.8	430.2
D1004		(500MHz, DMSO) δ 12.96 (bs, 1H), 7.53 (d, J = 7.4 Hz, 2H), 7.46 (dd, J = 10.5, 4.9 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 3.01 (tt, J = 10.9, 3.6 Hz, 1H), 2.32 (s, 3H), 2.08 – 2.01 (m, 2H), 1.80 – 1.73 (m, 2H), 1.69 – 1.53 (m, 3H), 1.46 – 1.37 (m, 2H), 1.34 – 1.24 (m, 1H).	99.9	444.2
D1005		(500MHz, DMSO)δ 7.52 – 7.46 (m, 4H), 7.41 (t, J = 6.7 Hz, 1H), 3.29-3.22 (m, 1H), 2.36 (s, 3H), 1.35 (d, J = 6.9 Hz, 6H).	97.3	404.1

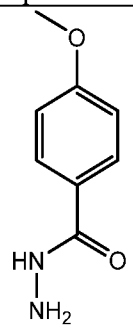
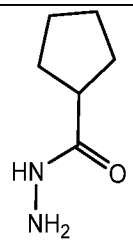
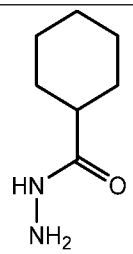
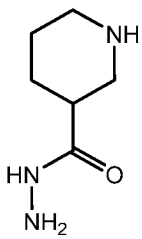
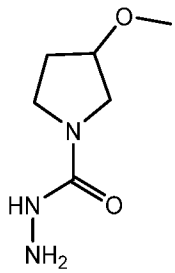
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1006	 (Forms thiadiazole)	(500MHz, DMSO) δ 12.99 (s, 1H), 7.57 – 7.41 (m, 5H), 3.21 – 3.15 (m, 1H), 2.81 (s, 3H), 2.13 – 2.06 (m, 2H), 1.84 – 1.77 (m, 2H), 1.74 – 1.67 (m, 1H), 1.58 (ddd, J = 24.2, 12.5, 3.2 Hz, 2H), 1.44 (ddt, J = 25.3, 12.6, 3.3 Hz, 2H), 1.35 – 1.25 (m, 1H).	100	460.2
D1007		(500 MHz, DMSO) δ 8.06 (dd, J = 1.7, 0.7 Hz, 1H), 7.59 (d, J = 7.5 Hz, 2H), 7.46 – 7.39 (m, 2H), 7.34 – 7.25 (m, 2H), 6.81 (dd, J = 3.5, 1.8 Hz, 1H), 2.35 (s, 3H).	99.4	428.0
D1008		1H NMR (500 MHz, DMSO) δ 13.08 (s, 1H), 7.67 (s, 1H), 7.52 – 7.40 (m, J = 25.2 Hz, 5H), 2.37 (s, 3H), 1.84 (s, 3H).	96.3	474.1
D1009		(500MHz, DMSO) δ 7.51 (d, J = 7.3 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 3.76 – 3.70 (m, 4H), 3.44 – 3.39 (m, 4H), 2.32 (s, 3H).	97.9	447.2
D1011		1H NMR (500 MHz, DMSO) δ 13.07 (s, 1H), 8.11 – 7.98 (m, 2H), 7.73 – 7.60 (m, 3H), 7.59 – 7.42 (m, 5H), 2.54 (s, 3H).	99.2	438.2
D1012		1H NMR (500 MHz, DMSO) δ 13.02 (s, 1H), 7.52 – 7.40 (m, 5H), 5.22 (dd, J = 7.7, 5.5 Hz, 1H), 3.96 – 3.81 (m, 2H), 2.40 (s, 3H), 2.38 – 2.23 (m, 2H), 2.13 – 1.97 (m, 2H).	99.5	432.2

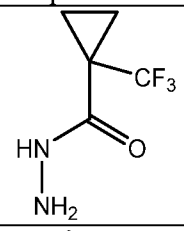
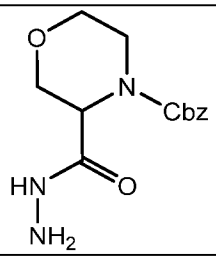
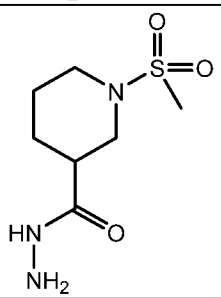
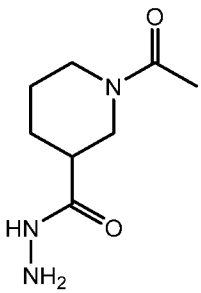
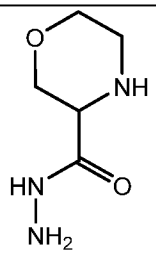
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1013		1H NMR (500 MHz, DMSO) δ 13.00 (s, 1H), 7.54 – 7.40 (m, 5H), 4.11 – 3.98 (m, 1H), 3.97 – 3.75 (m, 4H), 2.43 – 2.32 (m, 4H), 2.28 – 2.20 (m, 1H).	96.3	432.2
D1014		(500MHz, DMSO) δ 12.85 (bs, 1H), 7.55 – 7.44 (m, 4H), 7.37 (t, J = 7.2 Hz, 1H), 3.43 (bs, 4H), 2.29 (s, 3H), 1.96 (s, 4H).	99.4	431.9
D1015		(500 MHz, DMSO) δ 12.99 (s, 1H), 7.61 – 7.39 (m, 5H), 4.07 (dd, J = 11.1, 2.9 Hz, 1H), 3.82 – 3.74 (m, 1H), 3.71 – 3.64 (m, 1H), 3.55 – 3.45 (m, 1H), 3.29 – 3.20 (m, 1H), 2.42 (s, 3H), 2.20 – 2.10 (m, 1H), 1.99 – 1.86 (m, 1H), 1.77 – 1.70 (m, 1H), 1.68 – 1.55 (m, 1H).	97.7	446.2
D1016		(500 MHz, DMSO) δ 13.23 – 12.65 (m, 1H), 7.56 – 7.28 (m, 5H), 3.99 – 3.78 (m, 2H), 3.54 – 3.44 (m, 2H), 2.36 (d, J = 16.9 Hz, 3H), 2.07 – 1.96 (m, 2H), 1.86 – 1.67 (m, 2H).	97.4	446.2
D1017	 Also replace **I-1** with 	(500 MHz, DMSO) 3.29 – 3.19 (m, 1H), 3.03 – 2.96 (m, 1H), 2.45 – 2.31 (m, 3H), 2.07 – 2.00 (m, 2H), 1.92 – 1.80 (m, 5H), 1.79 – 1.71 (m, 2H), 1.69 – 1.52 (m, 5H), 1.46 – 1.36 (m, 2H), 1.33 – 1.22 (m, 2H).	95.0	436.2

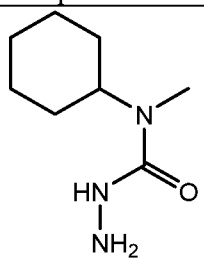
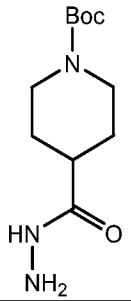
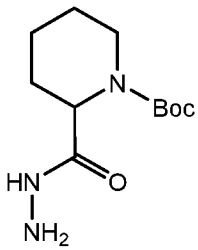
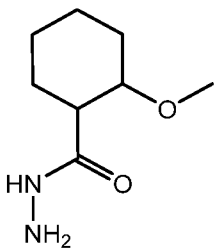
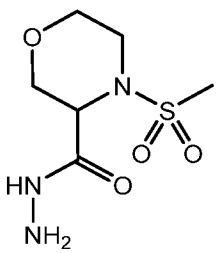
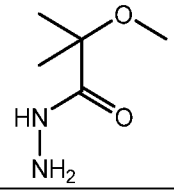
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1018	 Also replace **I-2** with 	^{1}H NMR (500 MHz, DMSO) δ 7.58 (d, J = 7.4 Hz, 2H), 7.45 – 7.40 (m, 2H), 7.33 – 7.28 (m, 1H), 4.31 (s, 2H), 3.41 – 3.35 (m, 1H), 3.07 (s, 3H), 2.11 – 2.03 (m, 2H), 1.90 – 1.81 (m, 2H), 1.78 – 1.62 (m, 4H).	96.5	460.2
D1019		(500 MHz, DMSO) δ 12.95 (s, 1H), 7.52 – 7.30 (m, 5H), 4.67 (s, 2H), 3.33 (s, 3H), 2.37 (s, 3H).	95.1	406.1
D1020		(500 MHz, DMSO) δ 12.89 (s, 1H), 7.54 – 7.45 (m, 5H), 3.44 (bs, 4H), 2.40 (s, 3H), 1.61 (bs, 6H).	99.3	445.2
D1021 Iso-1		(500 MHz, DMSO) δ 8.28 (s, 1H), 7.57 (d, J = 7.5 Hz, 2H), 7.41 (t, J = 7.7 Hz, 2H), 7.28 (t, J = 6.9 Hz, 1H), 3.28 (s, 3H), 3.06 – 2.97 (m, 1H), 2.41 (d, J = 15.4 Hz, 1H), 2.24 (s, 3H), 2.04 (d, J = 11.8 Hz, 2H), 1.88 – 1.78 (m, 1H), 1.48 – 1.31 (m, 3H), 1.17 – 1.07 (m, 1H). (Isomer 1)	99.1	747.1
D1021 Iso-2		(Also isolated Isomer 2)		

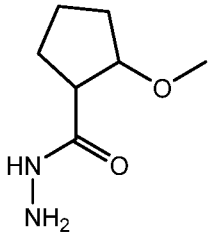
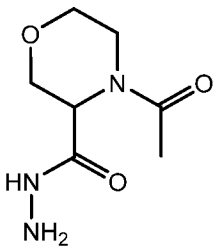
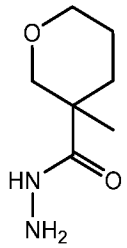
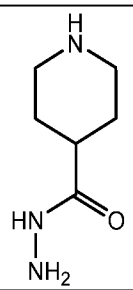
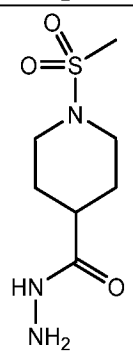
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1022		(500 MHz, DMSO) δ 12.88 (s, 1H), 7.53 – 7.46 (m, 4H), 7.45 – 7.39 (m, 1H), 3.98 – 3.90 (m, 1H), 3.56 – 3.49 (m, 1H), 3.46 – 3.39 (m, 1H), 2.35 (s, 3H), 2.18 – 2.08 (m, 1H), 2.06 – 1.98 (m, 1H), 1.96 – 1.87 (m, 1H), 1.69 – 1.62 (m, 1H), 1.26 (d, J = 6.3 Hz, 3H).		445.2
D1023		(500 MHz, CDCl3) δ 7.27 – 7.06 (m, 5H), 2.68 (s, 3H), 2.27 – 2.17 (m, 2H), 1.84 – 1.69 (m, 6H), 1.49 (s, 3H).	99.6	444.2
D1024		(500 MHz, CDCl3) δ 7.31 (s, 1H), 7.17 (d, J = 25.4 Hz,4H), 4.72 (dd, J = 10.2, 2.7 Hz, 1H), 4.02 (d, J = 11.3 Hz, 1H), 3.56 (t, J = 10.6 Hz, 1H), 2.78 (s, 3H), 2.11 – 1.90 (m, 3H), 1.61 (m, 3H).	98.9	446.2
D1025		(500 MHz, DMSO) δ 13.00 (s, 1H), 7.58 – 7.32 (m, J = 16.0 Hz, 5H), 4.07 (dd, J = 11.1, 2.8 Hz, 1H), 3.81 – 3.75 (m, 1H), 3.69 (dd, J = 11.1, 8.6 Hz, 1H), 3.55 – 3.45 (m, 1H), 3.29 – 3.20 (m, 1H), 2.37 (dd, J = 6.6, 4.7 Hz, 3H), 2.18 (dd, J = 13.1, 5.3 Hz, 1H), 1.97 – 1.87 (m, 1H), 1.74 (dd, J = 9.0, 4.6 Hz, 1H), 1.69 – 1.59 (m, 1H).	98.3	446.2
D1026		(500 MHz, DMSO) δ 13.00 (s, 1H), 7.60 – 7.38 (m, 5H), 4.07 (dd, J = 11.1, 2.9 Hz, 1H), 3.83 – 3.75 (m, 1H), 3.69 (dd, J = 11.2, 8.5 Hz, 1H), 3.55 – 3.48 (m, 1H), 3.30 – 3.23 (m, 1H), 2.42 (s, 3H), 2.22 – 2.11 (m, 1H), 1.99 – 1.87 (m, 1H), 1.74 (dd, J = 8.8, 4.4 Hz, 1H), 1.70 – 1.58 (m, 1H).	99.5	446.2

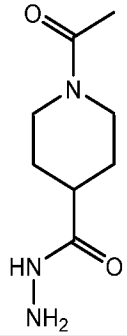
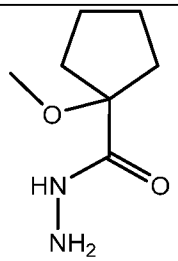
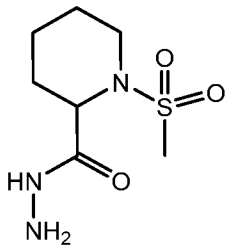
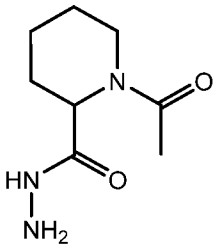
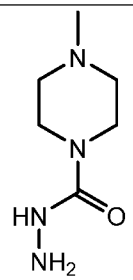
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1027		(500 MHz, DMSO) δ 12.82 (s, 1H), 7.46 (d, J = 7.4 Hz, 2H), 7.39 (t, J = 7.7 Hz, 2H), 7.29 (t, J = 7.6 Hz, 1H), 3.54 (d, J = 10.5 Hz, 1H), 3.39 – 3.27 (m, 5H), 3.22 (s, 3H), 2.22 (s, 3H), 1.84 – 1.77 (m, 1H), 1.77 – 1.69 (m, 1H), 1.55 – 1.47 (m, 1H), 1.43 (m, 1H).		475.2
D1028		(500 MHz, DMSO) δ 8.15 (s, 1H), 7.60 – 7.51 (m, 7H), 7.42 (t, J = 7.7 Hz,2H), 7.29 (t, J = 7.4 Hz, 1H), 3.44 (s, 3H), 2.35 (s, 3H).	95.5	550.2
D1029		(500 MHz, DMSO) δ 8.13 (s, 1H), 7.59 – 7.39 (m, 10H), 3.45 (s, 3H), 2.35 (s, 3H).	98.9	550.2
D1030	 Also replace **I-1** with 	(500 MHz, DMSO) δ 12.52 (s, 1H), 7.62-7.54 (m, 2H), 7.46 (t, J = 7.3 Hz, 2H), 7.34-7.28 (m, 1H), 4.06 (dd, J = 11.3, 3.8 Hz, 1H), 3.82 – 3.76 (m, 1H), 3.67 (dd, J = 11.1, 8.7 Hz, 1H), 3.52 – 3.46 (m, 1H), 3.27-3.20 (m, 1H), 2.38-2.31 (m, 6H), 2.20-2.13 (m, 1H), 1.96 – 1.86 (m, 1H), 1.78 – 1.70 (m, 1H), 1.68 – 1.60 (m, 1H).	98.9	392.2
D1031		(500 MHz, DMSO) δ 13.00 (s, 1H), 7.54 – 7.44 (m, 5H), 4.10-4.03 (m, 1H), 3.73-3.66 (m, 1H), 3.21 – 3.14 (m, 1H), 3.07 (t, J = 10.4 Hz, 1H), 2.41 (s, 3H), 2.19 – 2.11 (m, 1H), 1.88 – 1.76 (m, 3H), 1.56-1.47 (m, 1H), 1.39 (s, 9H).	98.5	545.4

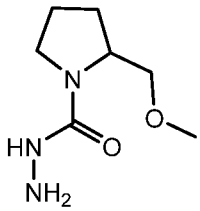
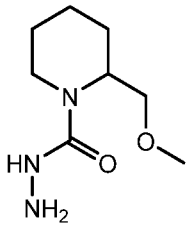
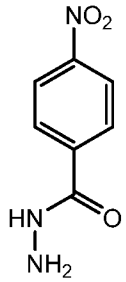
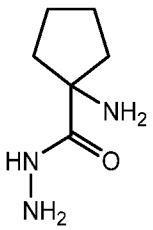
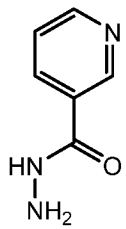
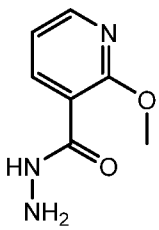
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1033	 Also replace **I-4** with **I-8**	(500MHz, DMSO) δ 12.38 (s, 1H), 7.91 – 7.87 (m, 2H), 7.53-7.43 (m, 5H), 7.14 – 7.10 (m, 2H), 4.23 (s, 2H), 3.84 (s, 3H), 2.47 (s, 3H).	99.9	482.1
D1034	 Also replace **I-4** with **I-8**	(400MHz, DMSO) δ 12.37 (s, 1H), 7.54 – 7.48 (m, 2H), 7.48 – 7.42 (m, 3H), 4.11 (s, 2H), 3.33 – 3.22 (m, 1H), 2.40 (s, 3H), 2.08 – 1.95 (m, 2H), 1.85 – 1.55 (m, 6H).	98.9	444.0
D1035	 Also replace **I-4** with **I-8**	(400MHz, DMSO) δ 12.37 (s, 1H), 7.55 – 7.42 (m, 5H), 4.11 (s, 2H), 2.89 (tt, J = 10.9, 3.7Hz, 1H), 2.41 (s, 3H), 2.01 – 1.90 (m, 2H), 1.78 – 1.67 (m, 2H), 1.67 – 1.58 (m, 1H), 1.54 – 1.42 (m, 2H), 1.42 – 1.17 (m, 3H).	99.4	458.0
D1036		(500 MHz, DMSO) δ 8.82-8.50 (m, 2H), 7.57 (d, J = 7.4 Hz, 2H), 7.44-7.38 (m, 2H), 7.31-7.26 (m, 1H), 3.67 – 3.62 (m, 1H), 3.49 – 3.41 (m, 1H), 3.28 – 3.24 (m, 2H), 3.03-2.94 (m, 1H), 2.29 (s, 3H), 2.22 – 2.16 (m, 1H), 1.92-1.73 (m, 3H).	99.5	445.2
D1037		(500 MHz, DMSO) δ 7.55 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 4.12 – 4.08 (m, 1H), 3.59 – 3.41 (m, 4H), 3.28 (s, 3H), 2.27 (s, 3H), 2.11 – 2.05 (m, 2H).	100	461.3

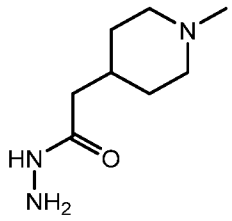
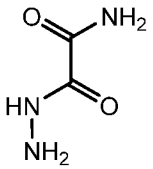
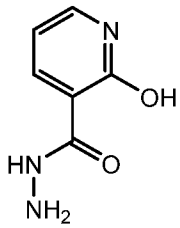
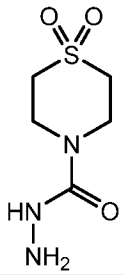
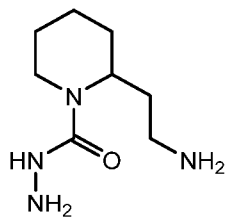
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1038		(500 MHz, DMSO) δ 7.53 – 7.45 (m, 4H), 7.40 (t, J = 7.1 Hz, 1H), 2.39 (s, 3H), 1.73 – 1.61 (m, 4H).	98.8	470.1
D1039		(500 MHz, $CDCl_3$) δ 7.39 – 7.11 (m, 10H), 5.43 (d, J = 34.8 Hz, 1H), 5.17 (d, J = 34.7 Hz, 2H), 4.43 (d, J = 9.8 Hz,1H), 3.91 (m, 3H), 3.60 (m, 2H), 2.69 (s,3H).	98.4	581.2
D1040		(500 MHz, DMSO) δ 13.00 (s, 1H), 7.55 – 7.41 (m, 5H), 3.82 (dd, J = 11.6, 3.3 Hz, 1H), 3.50-3.43 (m, 1H), 3.17 (dd, J = 11.6, 9.7 Hz, 1H), 2.92 (s, 3H), 2.37 (s, 3H), 2.19 – 2.12 (m, 1H), 1.91 – 1.84 (m, 1H), 1.82 – 1.73 (m, 1H), 1.72-1.62 (m, 1H).	97.8	523.3
D1041		Mixture of rotamers : (500 MHz, DMSO) δ 12.98 (s, 1H), 7.54-7.45 (m, 4H), 7.42-7.36 (m, 1H), 4.48 (d, J = 10.1 Hz, 0.5H), 3.94 (dd, J = 13.8, 3.4 Hz, 0.5H), 3.78 – 3.71 (m, 1H), 3.66 (dd, J = 13.7, 8.0 Hz, 0.5H), 3.23-3.17 (m, 1H), 3.12-3.01 (m, 1H), 2.35 (s, 3H), 2.23 – 2.08 (m, 1H), 2.07-2.00 (m, 3H), 1.96 – 1.89 (m, 0.5H), 1.88-1.81 (m,1H), 1.72 – 1.45 (m, 2H).	99.5	487.2
D1042		(500 MHz, DMSO) δ 8.13 (s, 1H), 7.57 (d, J = 7.5 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.31 (m, 1H), 6.52 (s, 1H), 4.15 (m, 1H), 3.91 – 3.79 (m, 32H), 3.71 – 3.63 (m, 1H), 3.19 (m, 1H), 3.07 (m, 1H), 2.30 (s, 3H).	98.4	447.1

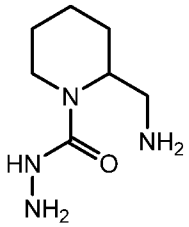
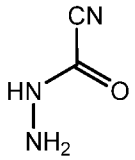
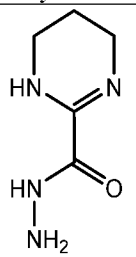
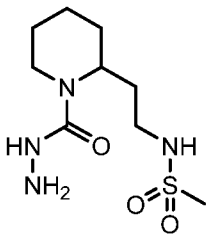
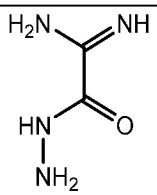
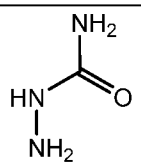
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1043		(500 MHz, DMSO) δ 12.88 (s, 1H), 7.53 – 7.48 (m, 4H), 7.47 – 7.41 (m, 1H), 3.75 – 3.63 (m, 1H), 2.95 (s, 3H), 2.36 (s, 3H), 1.85 – 1.72 (m, 4H), 1.66 – 1.52 (m, 3H), 1.38 – 1.27 (m, 2H), 1.20 – 1.07 (m, 1H).	100	473.3
D1044		(500 MHz, DMSO) δ 12.98 (s, 1H), 7.54 – 7.43 (m, 5H), 3.93 (d, J = 13.1 Hz, 2H), 3.30-3.24 (m, 1H), 3.06-2.97 (m, 2H), 2.41 (s, 3H), 2.05 (dd, J = 13.1, 3.1 Hz, 2H), 1.69-1.60 (m, 2H), 1.42 (s, 9H).	98.3	543.5 (M-H)
D1045		(500 MHz, DMSO) δ 13.10 – 12.93 (m, 1H), 7.52 – 7.41 (m, 5H), 5.61-5.52 (m, 1H), 4.70-4.58 (m, 1H), 4.17-4.09 (m, 1H), 3.94 (d, J = 13.2 Hz, 1H), 2.41 (s, 3H), 2.20 (d, J = 13.9 Hz, 1H), 1.91-1.83 (s, 1H), 1.72-1.58 (m, 3H), 1.42 (s, 9H).	95.7	543.4 (M-H)
D1046		(500 MHz, DMSO) δ 8.34 (s, 1H), 7.58 (d, J = 7.2 Hz, 2H), 7.45 – 7.36 (m, 2H), 7.30 – 7.21 (m, 1H), 3.19 (s, 3H), 2.99-2.96 (m,1H), 2.21 (s, 3H), 2.17-2.15 (m, 1H), 2.10-2.08 (m, 3H), 1.98-1.95 (m, 1H), 1.81 – 1.74 (m, 1H), 1.72-1.68 (m, 1H), 1.35-1.33 (m, 2H).	99.1	474.3
D1047		(500 MHz, DMSO) δ 8.20 (s, 1H), 7.58 (d, J = 7.3 Hz, 2H), 7.45 – 7.39 (m, 2H), 7.31 – 7.25 (m, 1H), 5.23 (s, 1H), 4.24 (d, J = 11.2 Hz, 1H), 3.92 (d, J = 11.6 Hz, 1H), 3.86 (dd, J = 12.0, 3.4 Hz, 1H), 3.61 – 3.47 (m, 3H), 3.07 (s, 3H), 2.33 (s, 3H).	98.9	525.3
D1048		(500 MHz, $CDCl_3$) δ 7.19 (m, 5H), 3.23 (s, 3H), 2.73 (s, 3H), 1.72 (s, 6H).	98.6	434.2

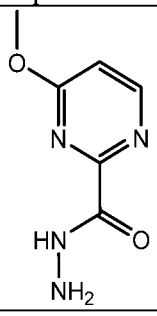
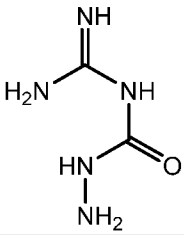
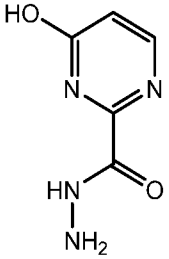
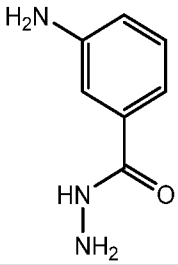
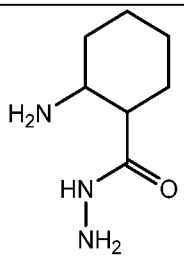
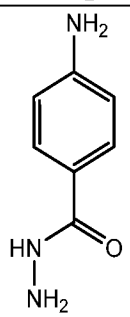
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1049		(500 MHz, DMSO) δ 12.97 (s, 1H), 7.46-7.53 (m, 5H), 4.07 (dt, J = 6.3, 4.2 Hz, 1H), 3.43 – 3.37 (m, 1H), 3.27 (s, 3H), 2.42 (s, 3H), 2.22-2.19 (m 1H), 1.97 – 1.86 (m, 2H), 1.80 – 1.66 (m, 3H).	99.8	460.3
D1050		(500 MHz, DMSO) δ 8.26 (s, 1H), 7.58 (d, J = 7.4 Hz, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.28 (t, J = 7.4 Hz, 1H), 5.68 (d, J = 2.9 Hz, 0.6H), 5.48 (s, 0.4H), 4.26-4.35 (m, 1H), 4.14 (d, J = 2.9 Hz, 0.5H) 3.89-3.75 (m. 1.5H), 3.91 – 3.80 (m, 1.5H), 3.78 – 3.74 (m, 1H), 3.61 – 3.51 (m, 2H), 2.87-2.92 (m, 0.5H), 2.30 (s, 1H), 2.26 (s, 2H), 2.13 (3H).	98.1	489.3
D1051		(500 MHz, DMSO) δ 12.97 (s, 1H), 7.49 (dd, J = 10.3, 2.8 Hz, 4H), 7.46 – 7.41 (m, 1H), 4.06 – 4.00 (m, 1H), 3.71 – 3.66 (m, 1H), 3.61 – 3.58 (m, 1H), 3.57 – 3.48 (m, 2H), 2.38 (s, 3H), 2.32 – 2.26 (m, 1H), 1.80 – 1.70 (m, 2H), 1.62 (m, 1H), 1.30 (s, 3H).	95.6	460.2
D1052		(500 MHz, DMSO) δ 7.51 (d, J = 7.3 Hz, 2H), 7.38 – 7.32 (m, 2H), 7.24 – 7.18 (m, 1H), 3.33 – 3.27 (m, 3H), 2.98 (td, J = 12.5, 3.0 Hz, 2H), 2.21 (s, 3H), 2.13 (dd, J = 14.2, 3.3 Hz, 2H), 1.89 – 1.80 (m, 2H).	100	445.2
D1053		(500 MHz, DMSO) δ 13.00 (s, 1H), 7.54 – 7.42 (m, 5H), 3.60 (td, J = 8.7, 3.7 Hz, 2H), 3.27-3.21 (m, 1H), 2.98 (td, J = 12.1, 2.7 Hz, 2H), 2.91 (s, 3H), 2.41 (s, 3H), 2.19 (dd, J = 13.5, 3.5 Hz, 2H), 1.88 – 1.78 (m, 2H).	98.4	523.2

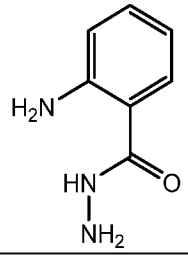
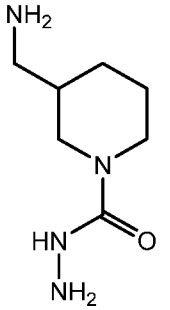
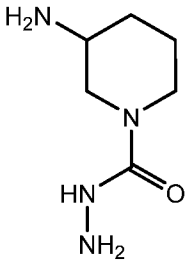
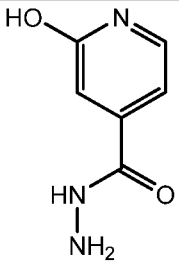
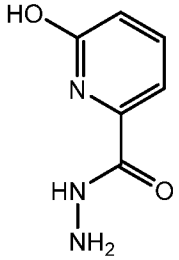
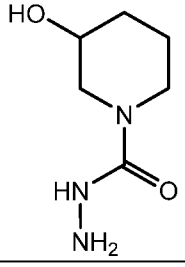
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1054		(500 MHz, DMSO) δ 7.56 (d, J = 7.6 Hz, 2H), 7.44-7.40 (m, 2H), 7.31-7.27 (m, 1H), 4.32-4.25 (m, 1H), 3.88-3.82 (m, 1H), 3.28-3.25 (m, 2H), 2.91-2.83 (m, 1H), 2.30 (s, 3H), 2.12-2.05 (m, 2H), 2.03 (s, 3H), 1.79-1.70 (m, 1H), 1.64-1.55 (m, 1H).	99.3	487.2
D1055		(500 MHz, DMSO) δ 13.02 (s,1H), 7.56 – 7.42 (m, 5H), 3.12 (s, 3H), 2.44 (s, 3H), 2.21 – 2.11 (m, 4H), 1.84 – 1.69 (m, 4H).	99.3	460.3
D1056		(500 MHz, DMSO) δ 7.55 (d, J = 7.5 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 5.39 (d, J = 3.7 Hz, 1H), 3.69-3.63 (m, 1H), 3.09 (td, J = 12.8, 2.4 Hz, 1H), 3.03 (s, 3H), 2.37 (s, 3H), 2.23-2.17 (m, 1H), 1.98-1.89 (m, 1H), 1.75-1.69 (m, 2H), 1.67 – 1.46 (m, 2H).	100	523.2
D1057		(500 MHz, DMSO)(mixture of rotamers) δ 7.58 (d, J = 7.2 Hz, 2H), 7.44-7.40 (m, 2H), 7.31-7.27 (m, 1H), 6.01-5.96 (m, 1H), 5.60-5.55 (m, 1H), 4.44-4.37 (m, 1H), 3.87-3.80 (m, 1H), 3.25-3.18 (m, 1H), 2.30-2.23 (m, 3H), 2.17-2.10 (m, 3H), 1.81-1.64 (m, 2H), 1.52 (m, 2H).	100	487.3
D1058		(500 MHz, DMSO) δ 8.25 (s, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.41 (t, J = 7.7 Hz, 1H), 7.28 (t ,J = 7.4 Hz, 1H), 4.28 – 3.66 (m, 6H), 3.43 – 3.40 (m, 2H), 2.51 – 2.48 (m, 3H), 2.46 – 2.42 (m, 2H), 2.24 (s, 3H)	96	460.1

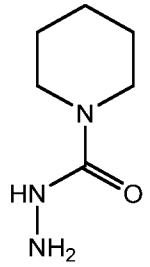
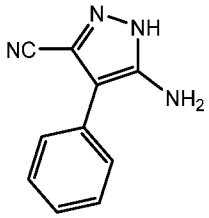
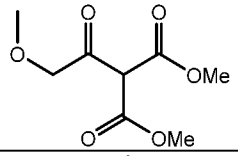
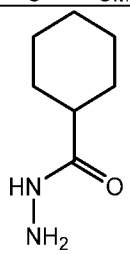
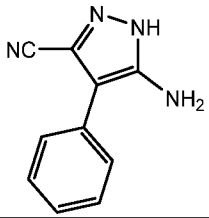
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1059		(500 MHz, DMSO) δ 8.20 (s, 1H), 7.64-7.60 (m, 2H), 7.48-7.43 (m, 2H), 7.36-7.28 (m, 1H), 3.97 (s, 1H), 3.53 – 3.50 (m, 1H), 3.44 – 3.40 (m, 3H), 3.28 (s, 3H), 2.31-2.22 (m, 3H), 2.03 – 1.88 (m, 4H)	99	475.2
D1060		(500 MHz, DMSO) δ 12.87 (s, 1H), 7.54 – 7.46 (m, 4H), 4.20 – 4.10 (m, 1H), 3.78 – 3.65 (m, 2H), 3.55 – 3.49 (m, 1H), 3.26 (s, 3H), 3.25 – 3.23 (m, 1H), 3.19 (d, J = 1.9 Hz, 1H), 2.38 (s, 3H), 1.74 – 1.51 (m, 6H)	98.8	489.2
D1061		(500 MHz, DMSO) δ 10.94 (s, 1H), 8.48 – 8.44 (m, 1H), 8.37 – 8.28 (m, 2H), 8.14 (d, J = 8.6 Hz, 1H), 7.51 (s, 2H), 7.41 – 7.31 (m, 3H), 3.32 (s, 3H)	95	483.1
D1062		(500 MHz, DMSO) δ 7.58 (d, J = 7.3 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.31 – 7.27 (m, 1H), 3.31 (s, 2H), 2.65 – 2.63 (m, 1H), 2.38 – 2.36 (m, 1H), 2.29 (s, 3H), 2.09 (s, 2H), 2.03 – 1.99 (m, 1H), 1.93 – 1.88 (m, 2H), 1.83 – 1.77 (m, 2H).	99.7	445.2
D1063		(500 MHz, DMSO) δ 9.12 (s, 1H), 8.71 (d, J = 4.3 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 7.60 – 7.56 (m, 1H), 7.52 – 7.48 (m, 2H), 7.36 – 7.32 (m, 2H), 7.21 (d, J = 7.3 Hz, 1H), 4.93 (s, 1H), 1.14 (s, 3H)	98.7	439.1
D1064		(500 MHz, DMSO) δ 8.39 (d, J = 3.4 Hz, 1H), 8.28 (d, J = 7.2 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.45 – 7.40 (m, 2H), 7.32 (t, J = 7.3 Hz, 1H), 7.23 – 7.18 (m, 1H), 3.97 (s, 3H), 2.36 (s, 3H)	98.4	468.9

Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1065		(500 MHz, DMSO) δ 9.12 (s, 1H), 7.59 (d, J = 7.4 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.32 – 7.28 (m, 1H), 3.43 (s, 1H), 3.29 – 3.20 (m, 1H), 2.94 (s, 3H), 2.76 (s, 3H), 2.29 (s, 3H), 2.11 – 1.93 (m, 3H), 1.62 – 1.45 (m, 2H), 1.31 – 1.21 (m, 1H)	96.8	473.1
D1066		(500 MHz, DMSO) δ 8.47 (s, 1H), 8.07 (s, 1H), 7.50 (d, J = 7.6 Hz, 2H), 7.43 – 7.30 (m, J = 7.6 Hz, 2H), 7.25 (t, J = 7.3 Hz, 1H), 2.28 (s, 3H). (ammonium salt)	99.7	405.0
D1067		(500 MHz, DMSO) δ 8.19 – 8.14 (m, 1H), 7.69 (d, J = 5.3 Hz, 1H), 7.60 (d, J = 7.4 Hz, 2H), 7.45 – 7.40 (m, 2H), 7.30 (t, J = 7.4 Hz, 1H), 7.09 (s, 2H), 6.42 (t, J = 6.6 Hz, 1H), 2.32 (s, 3H)	99.1	455.0
D1068		(500 MHz, DMSO) δ 12.91 (s, 1H), 7.54 – 7.45 (m, 5H), 3.98 – 3.89 (m, 4H), 3.38 – 3.34 (m, 4H), 2.45 (s, 3H)	97.9	495.0
D1069		(500 MHz, DMSO) δ 7.93 – 7.73 (m, 2H), 7.53 – 7.38 (m, 3H), 4.13 (s, 1H), 3.81 – 3.73 (m, 1H), 3.69 – 3.63 (m, 1H), 3.20 – 3.14 (m, 1H), 2.88 (s, 2H), 2.51 (s, 3H), 2.50 – 2.49 (m, 1H), 2.38 (s, 2H), 2.17 – 2.07 (m, 1H), 1.93 – 1.81 (m, 1H), 1.72 (s, 1H), 1.67 – 1.61 (m, 2H), 1.53 (s, 1H), 1.29 – 1.09 (m, 1H)	97	486.2 (M-H)

Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1070		(500 MHz, DMSO) δ 11.14 (s, 1H), 10.44 (s, 1H), 8.79 (s, 1H), 7.55 – 7.51 (m, 2H), 7.49 – 7.44 (m, 2H), 7.40 – 7.34 (m, 1H), 3.92 (d, J = 14.3 Hz, 2H), 3.76 (t, J = 9.3 Hz, 1H), 3.25 – 3.20 (m, 1H), 3.07 (t, J = 12.7 Hz, 1H), 2.55 (s, 3H), 1.84 (s, 2H), 1.73 (s, 1H), 1.46 (d, J = 8.2 Hz, 2H), 1.24 (s, 1H).	99.5	474.1
D1071	 Final step followed by primary amide dehydration	(500 MHz, DMSO) δ 13.53 – 12.91 (brs, 1H), 7.52 (s, 5H), 2.59 (s, 3H).	100	387.0
D1072		(500 MHz, DMSO) δ 13.53 – 12.91 (m, 1H), 7.52 (s, 5H), 2.59 (s, 3H).	99.1	443.9
D1073		(500 MHz, DMSO) δ 12.90 (s, 1H), 7.54 – 7.48 (m, 4H), 7.43 (s, 1H), 7.04 – 6.98 (m, 1H), 4.12 (s, 1H), 3.77 – 3.72 (m, 1H), 3.23 – 3.16 (m, 1H), 3.04 – 2.92 (m, 2H), 2.89 (s, 3H), 2.37 (s, 3H), 2.04 – 1.95 (m, 1H), 1.86 – 1.78 (m, 1H), 1.70 – 1.62 (m, 4H), 1.52 (s, 1H), 1.25 (s, 1H)	98.7	566.1
D1074		(500 MHz, DMSO) δ 9.78 (s, 3H), 7.63 – 7.53 (m, 2H), 7.48 – 7.39 (m, 2H), 7.36 – 7.23 (m, 1H), 2.40 (s, 3H).	97.9	404.1
D1075		(500 MHz, DMSO) δ 12.85 (s, 1H), 7.56 – 7.35 (m, 5H), 7.13 (s, 2H), 2.39 (s, 3H).	97.9	377.1

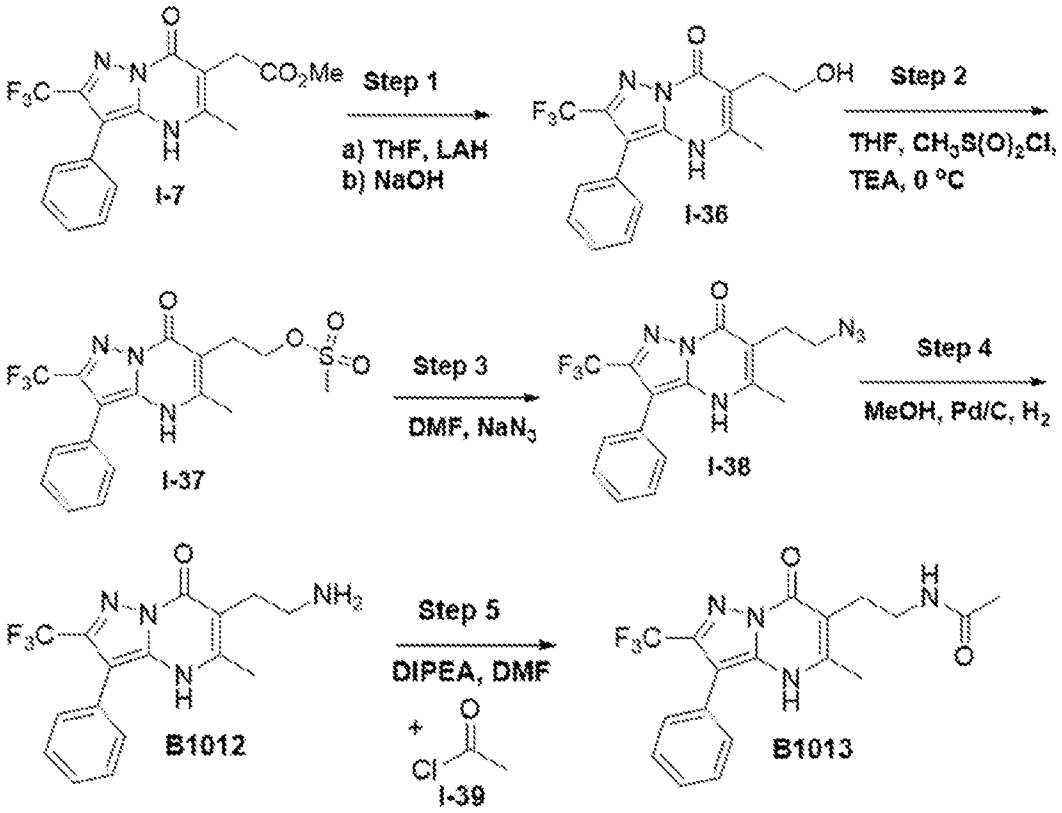
Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1076		(500 MHz, DMSO) δ 13.03 (s, 1H), 8.77 (d, J = 5.8 Hz, 1H), 7.56 – 7.45 (m, 5H), 7.19 (d, J = 5.8 Hz, 1H), 4.06 (s, 3H), 2.50 (s, 3H)	98.4	470.0
D1077		(500 MHz, DMSO) δ 7.59 (d, J = 7.4 Hz, 2H), 7.41 (t, J = 7.7 Hz, 2H), 7.27 (t, J = 7.4 Hz, 1H), 6.87 (br s, 4H), 2.19 (s, 3H).	96.1	419.0
D1078		(500 MHz, DMSO) δ 13.12 (s, 1H), 8.56 (s, 1H), 7.62 – 7.57 (m, 2H), 7.46 – 7.41 (m, 2H), 7.33 – 7.28 (m, 1H), 6.79 (s, 1H), 2.38 (s, 3H)	99.8	456.1
D1079		(500 MHz, DMSO) δ 8.35 (s, 1H), 7.62 – 7.59 (m, 2H), 7.45 – 7.41 (m, 2H), 7.32 – 7.26 (m, 2H), 7.17 – 7.14 (m, 1H), 7.07 – 6.97 (m, 1H), 6.79 – 6.75 (m, 1H), 5.49 (s, 2H), 2.34 (s, 3H)	96.2	453.1
D1080		(500 MHz, DMSO) δ 7.59 – 7.56 (m, 2H), 7.44 – 7.38 (m, 2H), 7.31 – 7.25 (m, 1H), 3.04 (s, 1H), 2.86 – 2.81 (m, 1H), 2.54 (s, 1H), 2.29 (s, 3H), 2.08 – 1.91 (m, 3H), 1.74 (s, 2H), 1.62 – 1.48 (m, 1H), 1.39 – 1.22 (m, 4H)	97.9	495.0
D1081		(500 MHz, DMSO) δ 8.48 (s, 1H), 7.70 – 7.65 (m, 2H), 7.62 – 7.58 (m, 2H), 7.45 – 7.41 (m, 2H), 7.31 – 7.27 (m, 1H), 6.71 – 6.67 (m, 2H), 5.85 (s, 2H), 2.30 (s, 3H)	95.8	453.1

Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1082		(500 MHz, DMSO) δ 8.20 (s, 1H), 7.67 – 7.63 (m, 1H), 7.56 (d, J = 7.4 Hz, 2H), 7.41 – 7.37 (m, 2H), 7.28 – 7.19 (m, 2H), 6.90 – 6.85 (m, 1H), 6.70 (s, 2H), 6.68 – 6.62 (m, 1H), 2.33 (s, 3H)	98.2	453.1
D1083		(500 MHz, DMSO) δ 7.60 – 7.57 (m, 2H), 7.44 – 7.40 (m, 2H), 7.31 – 7.26 (m, 1H), 3.95 – 3.91 (m, 1H), 3.80 – 3.72 (m, 2H), 3.22 – 3.14 (m, 1H), 3.11 – 3.03 (m, 1H), 2.92 – 2.76 (m, 4H), 2.55 (s, 1H), 2.22 (s, 3H), 1.97 – 1.84 (m, 2H), 1.31 – 1.21 (m, 1H), 1.13 – 1.04 (m, 1H)	95.6	474.1
D1084		(500 MHz, DMSO) δ 7.74 (s, 1H), 7.61 – 7.57 (m, 2H), 7.44 – 7.40 (m, 2H), 7.31 – 7.27 (m, 1H), 3.92 – 3.70 (m, 2H), 3.62 – 3.56 (m, 1H), 3.29 – 3.18 (m, 3H), 2.24 (s, 3H), 2.01 – 1.93 (m, 1H), 1.89-1.82 (m, 1H), 1.68 – 1.56 (m, 2H), 1.28 – 1.07 (m, 1H)	98.1	460.1
D1085		(500 MHz, DMSO) δ 11.98 (s, 1H), 7.65 – 7.60 (m, 1H), 7.60 – 7.55 (m, 2H), 7.48 – 7.43 (m, 2H), 7.36 – 7.31 (m, 1H), 6.88 – 6.85 (m, 1H), 6.77 – 6.70 (m, 1H), 2.55 (s, 1H), 2.44 (s, 3H)	97.4	455.1
D1086		(500 MHz, DMSO) δ 13.08 (s, 1H), 7.93 – 7.83 (m, 1H), 7.68 – 7.54 (m, 3H), 7.52 – 7.45 (m, 2H), 7.39 (s, 1H), 6.86 – 6.82 (m, 1H), 4.02 (s, 1H), 2.43 (s, 3H)	96.2	455.1
D1087		(500 MHz, DMSO) δ 7.53 – 7.41 (m, 5H), 5.01 (s, 1H), 3.76 – 3.68 (m, 1H), 3.67 – 3.53 (m, 2H), 3.28 – 3.23 (m, 1H), 3.22 – 3.13 (m, 1H), 3.04 – 2.96 (m, 1H), 2.35 (s, 3H), 1.92 – 1.77 (m, 2H), 1.58 – 1.37 (m, 2H).	97.0	461.1

Compound ID	Compound **I-35** replacement	^{1}H NMR	Purity (%)	MS (m/z)
D1088	 Also replace **I-1** with  Also replace **I-2** with 			
D1089	 Also replace **I-1** with 	(500 MHz, DMSO) δ 8.00 (d, *J* = 7.0 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.33 – 7.29 (m, 1H), 2.94 (s, 2H), 2.54 (s, 2H), 2.33 (s, 3H), 2.08 – 2.01 (m, 2H), 1.78 – 1.74 (m, 2H), 1.62 – 1.54 (m, 2H), 1.44 – 1.38 (m, 2H)	96.8	401.3

Example 18

[00479] Synthesis of 6-(2-aminoethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1012**) and *N*-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)ethyl)acetamide (**B1013**) was carried out in four and five steps, respectively, as follows:



[00480] Step 1: Synthesis of 6-(2-hydroxyethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-36**): Lithium aluminum hydride (457 µL, 12.4 mmol) was added to a white suspension of methyl 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)acetate (**I-7**, 2.27 g, 6.21 mmol, see Example 2) in THF (60 mL). The solution was stirred at r.t. for 1.5h. NaOH 2M (12 mL) was added and stirred at r.t. for 30 min. the mixture was filtered, washed with THF (2x15 mL), and the filtrate concentrated *in vacuo*. The crude material was purified by reverse phase chromatography (KP-C18-H5, 30 g, 0 to 100% MeCN in water 10mM ammonium formate over 20 column volumes) to afford the compound **I-36**. ^{1}HNMR (500MHz, DMSO) δ 12.09 (s, 1H), 7.55 – 7.20 (m, 5H), 4.61 (t, J = 5.6 Hz, 1H), 3.50 (dd, J = 12.6, 6.8 Hz, 2H), 2.67 (t, J = 6.9 Hz, 2H), 2.37 (s, 3H); MS (m/z): 338.0 $[M+1]^+$.

[00481] Step 2: Synthesis of 2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)ethyl methanesulfonate (**I-37**):Methanesulfonyl chloride (127 µL, 1.63 mmol) was added to a solution of **I-36** (500 mg, 1.48 mmol) and triethylamine (417 µL, 2.96 mmol) in THF (30 mL) at 0 °C. The solution was stirred at 0 °C for 1.5h. EtOAc (75 mL), water (50 mL) and HCl 10% (3 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 50 mL). The

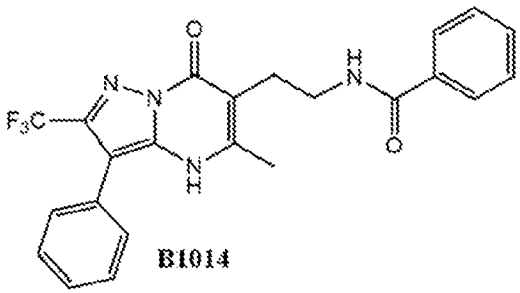
combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The solid was triturated with DCM (20 mL) for 15 min, filtered, washed with DCM (2 x 5 mL) and dried *in vacuo* to afford the compound **I-37**. ^{1}HNMR (500MHz, DMSO) δ 12.19 (s, 1H), 7.53 – 7.44 (m, 3H), 7.44 – 7.40 (m, 2H), 4.32 (t, J = 6.7 Hz, 2H), 3.17 (s, 3H), 2.94 (t, J = 6.7Hz, 2H), 2.40 (s 3H). MS (m/z): 416.0 $[M+1]^+$.

[00482] Step 3: Synthesis of 6-(2-azidoethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-38**):Sodium azide (37.7 µL, 578 µmol) was added to a solution of **I-37** (200 mg, 481 µmol) in DMF (3.00 mL). The solution was stirred at r.t. for 1h. EtOAc (25 mL), water (25 mL) and 10% HCl (1 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to afford compound **I-38**. ^{1}HNMR (400MHz, DMSO) δ 12.19 (s, 1H), 7.54 – 7.38 (m, 5H), 3.47 (t, J = 7.1 Hz, 2H), 2.79 (t, J = 7.1 Hz, 2H), 2.41 (s, 3H). MS (m/z): 363.2 $[M+1]^+$.

[00483] Step 4: Synthesis of 6-(2-aminoethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1012**):A mixture of **I-38** (162 mg, 447 µmol), palladium on carbon 10 % loading (200 mg, 188 µmol) in MeOH (10 mL) was hydrogenated under an atmosphere of hydrogen for 18h. The mixture was filtered through celite, washed with MeOH (2 x 10 mL) and concentrated *in vacuo* to afford compound **B1012**. ^{1}HNMR (400MHz, DMSO) δ 7.76 (s, 2H), 7.58 (d, J = 7.5 Hz, 2H), 7.38 (t, J = 7.7 Hz, 2H), 7.23 (t, J = 7.4 Hz, 1H), 2.93 (t, J = 7.1 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 2.26 (d, J = 6.9 Hz, 3H).

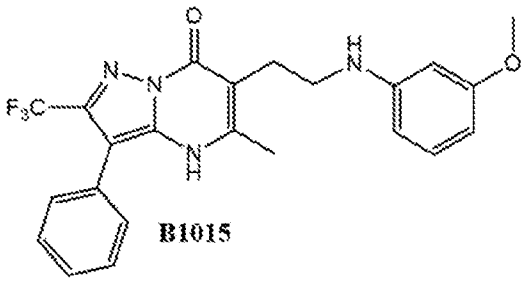
[00484] Step 5: Synthesis of *N*-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)ethyl)acetamide (**B1013**): Acetyl chloride (**I-39**,10.3 µL, 143 µmol) was added to a solution of **B1012** (40.0 mg, 119 µmol) and N,N-diisopropylethylamine (62.2 uL, 357 µmol) in DMF (2.00 mL). The yellow solution was stirred at r.t. for 17h. EtOAc (25 mL), water (25 mL) and 10% HCl (1 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and concentrated *in vazuo*. Purification by reverse phase chromatography (KP-C18-H5, 12 g, 0 to 100% MeCN in water 10mM ammonium formate over 40 column volumes) afforded compound **B1013**. ^{1}HNMR (500MHz, DMSO) δ 12.08 (s, 1H), 7.93 (t, J = 5.8 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.48 – 7.39 (m, 3H), 3.17 (dd, J = 13.5 Hz, 6.5 Hz, 2H), 2.62 (t, J = 7.1 Hz, 2H), 2.34 (s, 3H), 1.77 (s, 3H). MS (m/z): 379.1 $[M+1]^+$.

[00485] *N*-(2-(5-methyl-7-oxo-3-phenyl-2-(trifluoromethyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidin-6-yl)ethyl)benzamide (**B1014**)

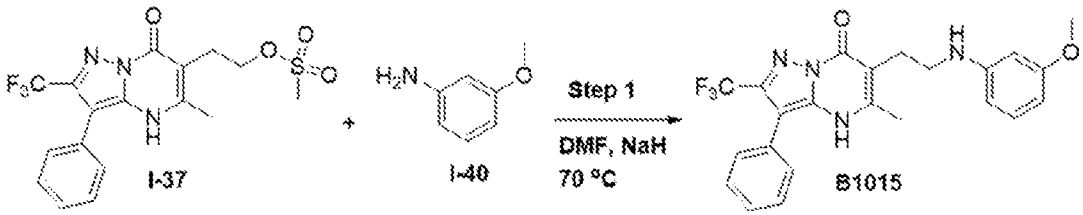


was prepared similarly, replacing **I-39** with benzoyl chloride in Step 5.

[00486] 6-(2-((3-methoxyphenyl)amino)ethyl)-5-methyl-3-phenyl-2-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**B1015**)



was prepared from compound **I-38** (from Step 2 above) in one step as follows:



[00487] **Step 1**: Sodium hydride (3.76 mg, 156 µmol) was added to a solution of **I-37** (50.0 mg, 120 µmol) and m-anisidine (**I-40**, 17.1 µL, 144 µmol) in DMF (1.00 mL). The solution was heated at 70 °C for 45 min. EtOAc (25 mL), water (25 mL), and 10% HCl (1 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by reverse phase chromatography (KP-C18-H5, 12 g, 0 to 100% MeCN in water 10mM ammonium formate over 20 column volumes) to afford Compound **B1015**. ^{1}HNMR (400MHz, DMSO) δ 8.17 (s, 1H), 7.54 (d, J = 7.6 Hz, 2H), 7.40 (t, J = 7.6 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 6.94 (t, J = 8.2 Hz, 1H), 6.23 – 6.15 (m, 2H), 6.10 – 6.03 (m, 1H), 5.79 (s, 1H), 3.67 (s, 3H), 3.15 – 3.05 (m, 2H), 2.75 (t, J = 7.2 Hz, 2H), 2.27 (s, 3H). MS (m/z): 443.1 $[M+1]^+$.

Example 19: Synthesis of Triazolopyrimidinone analogs.

[00488] Triazolopyrimidinone analogs of the pyrazolopyrimidine compounds described in the above Examples 1-18, e.g. compounds of Formula Ia, can be prepared following similar methods, where the starting aminopyrazole, e.g. compound **I-1** and similar starting materials used in Examples 1-18 can be replaced with the corresponding aminotriazole to provide the desired compounds. For example, 6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**E1001**) was prepared following the procedure of Example 4, starting with 4-phenyl-1H-1,2,3-triazol-5-amine (**I-41**) in place of 4-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-amine (**I-1**) in Step 1 of Example 3

[00489] **Step 1**: Synthesis of 5-methyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-42**): 4-phenyl-1*H*-1,2,3-triazol-5-amine (**I-41**) was reacted with ethyl acetoacetate (**I-10**) according to the methods described in Step 1 of Example 3 to provide the desired compound **I-42**.

[00490] **Step 2**: Synthesis of 6-iodo-5-methyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**I-43**): Compound **I-42** was reacted according to the methods described in Step 1 of Example 4 to provide the desired compound **I-43**.

[00491] **Step 3**: Synthesis of 6-(4-methoxybenzo[*d*]oxazol-2-yl)-5-methyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (**E1001**): Compound **I-43** was reacted with 4-methoxybenzo[d]oxazole (**I-15**) according to the methods described in Step 2 of Example 4 to provide the desired compound **E1001**. ^{1}HNMR (500 MHz, DMSO) δ 8.40 – 8.33 (m, 3H), 7.48 – 7.41 (m, 2H), 7.30 – 7.26 (m, 2H), 7.23 (t,J = 7.4 Hz, 1H), 6.94 – 6.89 (m, 1H), 4.02 (s, 3H), 2.49 (s, 3H). MS (m/z): 374.1 $[M+1]^+$, 94%.

Example 20: cGAS biochemical activity assay

[00492] Human cGAS sequence encoding amino acids 155-522 was cloned into a pET (EMD Millipore) based expression plasmid. The resulting construct contained a tandem N-terminal hexahistidine tag, maltose binding protein fusion followed by a tobacco etch virus protease cleavable linker preceding cGAS amino acids 155-522.

[00493] Construct sequence: Amino acids 155-522, Human cGAS

DAAPGASKLRAVLEKLKLSRDDISTAAGMVKGVVDHLLLRLKCDSAFRGVGLLNTG
SYYEHVKISAPNEFDVMFKLEVPRIQLEEYSNTRAYYFVKFKRNPKENPLSQFLEGEI
LSASKMLSKFRKIIKEEINDIKDTDVIMKRKRGGSPAVTLLISEKISVDITLALESKSSW
PASTQEGLRIQNWLSAKVRKQLRLKPFYLVPKHAKEGNGFQEETWRLSFSHIEKEILN
NHGKSKTCCENKEEKCCRKDCLKLMKYLLEQLKERFKDKKHLDKFSSYHVKTAFFH

VCTQNPQDSQWDRKDLGLCFDNCVTYFLQCLRTEKLENYFIPEFNLFSSNLIDKRSKE FLTKQIEYERNNEFPVFDEF, SEQ. ID No. 1

[00494] Protein was expressed and purified from *E. coli* BL21 DE3 Rosetta 2 (EMD Millipore) cells using standard techniques. Cells were grown in 2x yeast extract tryptone medium and expression was initiated via the addition of isopropyl β-D-1-thiogalactopyranoside. Expression proceeded overnight at 18°C. Cells were harvested by centrifugation and subsequently lysed via sonication. Insoluble fraction was removed by centrifugation. Maltose binding protein (MBP) fusion proteins were purified on a dextrin sepharose column (GE Healthcare) and the MBP tag was removed using tobacco etch virus protease overnight during dialysis. Protein was further purified on a heparin column (GE Healthcare) and eluted using a NaCl gradient. Column fraction were pooled and further purified on a Superdex 75 gel filtration column (GE Healthcare). Protein was quantified using 280nm absorbance. Protein was then flash frozen in liquid nitrogen and stored at -80°C until use.

[00495] Potential antagonists were diluted in 100% dimethyl sulfoxide and added to the reaction. Final dimethyl sulfoxide concentration was 5%. The compounds were tested from 1 μM with either 3- or 4-fold serial dilutions down to 0.000051 or 0.000004 μM respectively.

[00496] Two complementary DNA oligos (IDT DNA) were annealed by slow cooling from 95°C. The resulting double stranded DNA was used to activate cGAS.

[00497] Top strand oligo: 5'-TACAGATCTACTAGTGATCTATGACTGATCTGTACATGATCTACA-3' SEQ. ID No. 2

[00498] Bottom strand oligo: 3'-TGTAGATCATGTACAGATCAGTCATAGATCACTAGTAGATCTGTA-3' SEQ. ID No. 3

[00499] Reactions were performed at 37°C for 1.25 hours. Reaction buffer: 20mM Tris HCl pH 9, 100mM NaCl, 5 mM $MgCl_2$, 0.1 mg/ml bovine gamma globulin, 250 μM adenosine triphosphate, 100 μM guanosine triphosphate, 0.5 mM Tris(2-carboxyethyl)phosphine hydrochloride, 1 μM double stranded DNA and 300 nM purified cGAS protein.

[00500] Reactions were stopped and ATP levels in the reaction were measured using a luciferase based assay. Promega Kinase-Glo Max Assay. Luminescence was measured on a plate reader (Molecular Devices). Values were normalized to control wells lacking compound.

[00501] Table 15 below provides IC_{50} data for certain compounds of the invention on cGAS. "A" indicates an IC_{50} value between less than 20 μM, "B" indicates an IC_{50} value between 20 and 250 μM, and "C" indicates an IC_{50} above the upper limit of the assay (250 μM), or where an IC_{50} value could not be generated from the data.

Table 15

Compound ID	cGAS IC_{50} (μM)
A1001	B
A1002	A
A1003	C
A1004	C
A1005	B
A1006	A
A1007	B
A1008	B
A1009	C
A1010	B
A1011	C
A1012	B
A1013	C
A1014	B
A1015	B
A1016	B
A1017	A
A1018	B
A1019	C
A1020	B
A1021	B
A1022	A
A1023	B
A1024	A
A1025	B

Compound ID	cGAS IC_{50} (μM)
A1026	B
A1027	B
A1028	A
A1029	A
A1030	A
A1031	A
A1032	A
A1033	B
A1034	C
A1035	C
A1036	B
A1037	B
A1038	B
A1039	B
A1040	B
A1041	B
A1042	B
A1043	B
A1044	B
A1045	A
A1046	B
A1047	B
A1048	B
A1049	B
A1050	B

Compound ID	cGAS IC_{50} (μM)
A1051	A
A1052	B
A1053	B
A1054	B
A1055	B
A1056	A
A1057	B
A1058	B
A1059	A
A1060	B
A1061	B
A1062	A
A1063	A
A1064	A
A1065	A
A1066	A
A1067	A
A1068	B
A1069	A
A1070	A
A1071	B
A1072	B
A1073	B
A1074	A
A1075	A

Compound ID	cGAS IC_{50} (μM)
A1076	A
A1077	A
A1078	B
A1079	A
A1080	B
A1081	A
A1082	A
A1083	A
A1084	A
A1085	B
A1086	A
A1087	B
A1088	B
A1089	A
A1090	A
A1091	B
A1092	B
A1093	B
A1094	A
A1095	A
A1096	A
A1097	B
A1098	B
A1099	B
A1100	A
A1101	A
A1102	A
A1103	B
A1104	A
A1105	A

Compound ID	cGAS IC_{50} (μM)
A1106	A
A1107	A
A1108	B
A1109	B
A1110	A
A1111	A
A1112	A
A1113	B
A1114	C
A1115	B
A1116	A
A1117	B
A1118	B
A1119	B
A1120	A
A1121	A
A1122	B
A1123	C
A1124	A
A1125	A
A1126	C
A1127	A
A1128	A
A1129	A
A1130	B
A1131	B
A1132	A
A1133	A
A1134	A
A1135	A

Compound ID	cGAS IC_{50} (μM)
A1136	A
A1137	B
A1138	B
A1139	A
A1140	B
B1001	B
B1002	C
B1003	C
B1004	B
B1005	B
B1006	B
B1007	C
B1008	B
B1009	C
B1010	B
B1011	B
B1013	B
B1014	B
B1015	A
C1001	B
C1002	B
C1003	B
C1004	B
C1005	B
C1006	C
C1007	B
C1008	B
C1009	A
C1010	C
C1011	C

Compound ID	cGAS IC_{50} (μM)
C1012	C
C1013	C
C1014	A
C1015	C
C1016	A
C1017	A
C1018	A
C1019	A
C1020	B
C1021	B
C1022	A
C1023	A
C1024	A
C1025	A
C1026	B
C1027	A
C1028	C
C1029	B
C1030	A
C1032	A
C1033	A
C1034	C
C1035	C
C1036	C
C1037	A
C1038	A
C1039	A
C1040	A
C1041	A
C1042	A

Compound ID	cGAS IC_{50} (μM)
C1043	C
C1044	A
C1045	A
C1046	A
C1047	A
C1048	A
C1049	B
C1050	A
C1051	A
C1052	A
C1053	A
C1054	B
C1055	A
C1056	A
C1057	A
C1058	A
C1059	A
C1060	A
C1061	B
C1062	A
C1063	C
C1064	B
C1065	B
C1066	A
C1067	C
C1068	B
C1070	A
C1071	A
C1072	B
C1073	A

Compound ID	cGAS IC_{50} (μM)
C1074	B
C1075	A
C1076	A
C1077	A
C1078	A
C1079	C
C1080	B
C1081	A
C1082	A
C1083	C
C1084	A
C1085	A
C1086	C
C1087	B
C1088	A
C1089	A
C1090	B
C1091	A
C1092	A
C1093	A
C1094	A
C1095	A
C1096	A
C1097	A
C1098	A
C1099	A
C1100	A
C1101	A
C1102	B
C1103	A

Compound ID	cGAS IC_{50} (μM)
C1104	A
C1105	A
C1106	A
C1107	C
C1108	A
C1109	A
C1110	B
C1111	A
C1112	B
C1113	A
C1114	A
C1115	B
C1116	A
C1117	A
C1118	A
C1119	A
C1120	B
C1121	A
C1122	A
C1123	A
C1125	A
C1126	A
C1127	B
C1128	C
C1129	B
C1130	A
C1131	A
C1132	A
C1133	B
C1134	A

Compound ID	cGAS IC_{50} (μM)
C1135	A[1]
C1136	A
C1137	A
C1138	A
C1139	A
C1140	B
C1141	A
C1142	A
C1143	A
C1144	B
C1145	A
C1146	A
C1147	B
C1148	B
C1149	A
C1150	B
C1151	A
C1152	A
C1153	A
C1154	A
C1155	A
C1156	A
C1157	A
C1158	C
C1159	A
C1160	A
C1161	A
C1162	A
C1163	A
C1164	C

Compound ID	cGAS IC_{50} (μM)
C1165	A
C1166	A
C1167	A
C1168	B
C1169	A
C1170	A
C1171	B
C1172	A
C1173	A
C1174	A
C1175	A
C1176	B
C1177	A
C1178	A
C1179	B
C1180	A
C1181	A
C1182	A
C1183	A
C1184	A
C1185	A
C1186	B
C1187	A
C1188	A
C1189	B
C1190	B
C1191	C
C1192	A
C1193	A
C1194	A

Compound ID	cGAS IC_{50} (μM)
C1195	A
C1196	A
C1197	B
C1198	B
C1199	B
C1200	B
C1201	B
C1202	A
C1203	A
C1204	A
C1205	A
C1206	A
C1207	B
C1208	B
C1209	A
C1210	A
C1211	A
C1212	B
C1213	A
C1214	B
C1215	B
C1216	A
C1217	B
C1218	A
C1219	A
C1220	B
C1221	B
C1222	A
C1223	A
C1224	A

Compound ID	cGAS IC_{50} (μM)
C1225	A
C1226	A
C1227	A
C1228	B
C1229	B
C1230	A
C1231	B
C1232	A
C1233	A
C1234	A
C1235	B
C1236	A
C1237	B
C1238	B
C1239	A
C1240	A
C1241	A
C1242	C
C1243	A
C1244	A
C1245	A
C1246	A
C1247	A
C1248	A
C1249	A
C1250	A
C1251	A
C1252	A
C1253	A
C1254	A

Compound ID	cGAS IC_{50} (μM)
C1255	A
C1256	A
C1257	A
C1258	A
C1259	A
C1264	C
C1265	C
C1266	C
C1267	C
C1268	C
C1269	C
C1270	A
C1271	A
C1272	A
C1273	A
C1274	A
C1275	A
C1276	A
C1277	A
C1284	A
D1001	B
D1002	C
D1003	A
D1004	A
D1005	B
D1006	A
D1007	C
D1008	B
D1009	B
D1011	C

Compound ID	cGAS IC_{50} (μM)
D1012	A
D1013	B
D1014	A
D1015	B
D1016	A
D1017	C
D1018	A
D1019	A
D1020	A
D1021 Iso-1	A
D1021 Iso-2	A
D1022	A
D1023	A
D1024	A
D1025	A
D1026	A
D1027	A
D1028	A
D1029	A
D1030	A
D1031	B
D1032	B
D1033	B
D1034	B
D1035	B
D1036	B
D1037	A
D1038	A
D1039	B

Compound ID	cGAS IC_{50} (μM)
D1040	A
D1041	B
D1042	B
D1043	C
D1044	B
D1045	B
D1046 Iso-1	A
D1046 Iso-2	A
D1046 Iso-3	A
D1047	A
D1048	B
D1049 Iso-1	A
D1049 Iso-2	A
D1050	B
D1051	B
D1052	B
D1053	B
D1054	B
D1055	A
D1056	A
D1057	A
D1058	B
D1059	B
D1060	B
D1061	B
D1062	A
D1063	B

Compound ID	cGAS IC_{50} (μM)
D1064	C
D1065	B
D1066	A
D1067	A
D1068	B
D1069	B
D1070	A
D1071	A
D1072	A
D1073	A
D1074	A
D1075	B
D1076	B
D1077	A
D1078	A
D1079	C
D1080	C
D1081	C
D1082	B
D1083	B
D1084	A
D1085	A
D1086	A
D1087	B
D1089	A
E1001	A

[1]HCl salt of the insoluble free base (C1128)

Example 21: THP1 cell-based cGAS/STING pathway activity assay

[00502] A cellular assay can be used to assess the compounds of the invention for their ability to inhibit the cGAS/STING pathway. Cells that express a luciferase-based reporter that is linked to IRF-3 activation are used to determine response as a function of compound concentration. Such an assay is described in Vincent et al., Nature Communications 2017, 8(1):750, doi: 10.1038/s41467-017-00833-9. Compounds of the invention were assessed using similar assay methods in a THP1 cell assay to generate IC_{50} values as provided in the following Table 16. In this table, activity level "A" indicates an IC_{50} value less than 20 μM, "B" indicates an IC_{50} value between 20 and 100 μM, and "C" indicates an IC_{50} value above the upper limit of the assay (100 μM), or where an IC_{50} value could not be generated from the data.

Table 16

Compound ID	THP-1 IC_{50} (μM)
A1002	B
A1006	C
A1023	B
A1028	B
A1029	B
A1031	C
A1032	A
A1033	B
A1048	B
A1051	B
A1056	B
A1059	A
A1062	A
A1063	B
A1064	B
A1065	B
A1066	A

Compound ID	THP-1 IC_{50} (μM)
A1067	C
A1068	C
A1069	B
A1070	A
A1072	B
A1073	C
A1074	C
A1075	B
A1076	B
A1077	C
A1079	C
A1081	B
A1082	A
A1083	C
A1084	B
A1088	B
A1089	C

Compound ID	THP-1 IC_{50} (μM)
A1095	A
A1096	B
A1099	C
A1100	B
A1101	A
A1102	C
A1104	B
A1106	C
A1107	A
A1110	C
A1111	C
A1112	B
A1113	C
A1115	C
A1116	B
A1117	C
A1118	C

Compound ID	THP-1 IC_{50} (μM)
A1120	C
A1121	C
A1124	C
A1125	B
A1127	B
A1128	C
A1129	B
A1132	B
A1134	A
A1135	A
A1136	B
A1139	A
B1010	B
B1011	B
C1005	C
C1008	C
C1009	B
C1010	A
C1011	A
C1012	A
C1013	A
C1014	A
C1015	A
C1016	A
C1017	B
C1018	C
C1019	B
C1020	C
C1022	B

Compound ID	THP-1 IC_{50} (μM)
C1023	C
C1024	B
C1025	C
C1026	A
C1027	B
C1030	C
C1032	B
C1033	C
C1037	A
C1038	A
C1039	C
C1040	A
C1041	A
C1042	A
C1045	A
C1046	A
C1047	A
C1048	B
C1050	A
C1051	B
C1052	B
C1053	B
C1054	C
C1055	A
C1056	A
C1057	C
C1058	C
C1059	C
C1060	A

Compound ID	THP-1 IC_{50} (μM)
C1061	B
C1062	C
C1064	A
C1065	C
C1066	C
C1070	A
C1071	A
C1073	A
C1074	C
C1075	C
C1076	A
C1077	A
C1078	A
C1079	A
C1081	A
C1082	A
C1084	A
C1085	C
C1088	B
C1089	A
C1091	A
C1092	C
C1093	B
C1094	A
C1095	C
C1096	C
C1097	C
C1098	A
C1099	A

Compound ID	THP-1 IC_{50} (μM)
C1100	B
C1101	B
C1103	B
C1104	C
C1105	A
C1106	B
C1107	A
C1108	C
C1109	C
C1111	A
C1112	C
C1113	A
C1114	A
C1116	C
C1117	C
C1118	A
C1119	A
C1121	A
C1122	B
C1123	B
C1125	B
C1126	B
C1130	B
C1131	C
C1132	C
C1134	A
C1135	C
C1136	A
C1137	C

Compound ID	THP-1 IC_{50} (μM)
C1138	C
C1139	A
C1141	C
C1143	C
C1145	A
C1146	C
C1149	B
C1151	A
C1152	B
C1153	B
C1154	A
C1155	B
C1156	B
C1157	A
C1159	C
C1160	C
C1161	A
C1162	A
C1163	C
C1165	C
C1166	B
C1167	A
C1169	B
C1170	C
C1173	B
C1174	C
C1175	B
C1177	B
C1178	A

Compound ID	THP-1 IC_{50} (μM)
C1180	C
C1181	C
C1182	C
C1183	A
C1184	C
C1185	B
C1187	C
C1188	A
C1193	C
C1194	C
C1195	C
C1202	B
C1203	C
C1204	C
C1205	C
C1206	C
C1209	C
C1211	C
C1213	B
C1216	C
C1218	C
C1219	C
C1222	B
C1223	B
C1224	C
C1226	B
C1227	C
C1229	A
C1230	C

Compound ID	THP-1 IC_{50} (μM)
C1231	A
C1232	B
C1233	A
C1234	C
C1240	A
C1241	A
C1243	A
C1244	A
C1245	C
C1246	C
C1248	C
C1249	C
C1250	C
C1251	C
C1252	C
C1253	B
C1254	C
C1255	C
C1256	C
C1257	C
C1258	A
C1259	C
C1269	B
C1271	C
C1272	A

Compound ID	THP-1 IC_{50} (μM)
C1273	A
C1274	C
C1275	C
D1004	C
D1007	B
D1008	C
D1012	C
D1014	C
D1015	C
D1016	C
D1018	B
D1019	C
D1020	C
D1021 Iso-1	B
D1021 Iso-2	C
D1022	C
D1023	C
D1024	C
D1025	B
D1026	C
D1027	C
D1028	C
D1029	C
D1030	C

Compound ID	THP-1 IC_{50} (μM)
D1038	A
D1040	C
D1041	C
D1042	C
D1046 Iso-1	A
D1046 Iso-3	C
D1047	C
D1048	C
D1049 Iso-2	C
D1050	C
D1051	C
D1055	B
D1056	C
D1057	B
D1062	C
D1070	C
D1071	A
D1072	C
D1077	C
D1078	C
D1085	C
D1086	C

Example 22: Inhibition of cytokine secretion by Trex1-knockout (KO) bone marrow-derived macrophages (BMMs)

[00503] The inhibition of secreted cytokine was measured in bone marrow-derived macrophages (BMMs) from diseased mice to evaluate the potency of compounds of the

invention as described herein. Mice lacking the gene for Trex1 protein (*trex1-/-* or Trex1-KO) exhibit cGAS/STING pathway-dependent autoimmune and autoinflammatory disease manifestations, including enhanced cytokine secretion by cells. To derive bone marrow macrophages, marrow extracted from the femurs and tibias were harvested from Trex1-KO mice was cultured in growth media supplemented with macrophage colony-stimulating factor (M-CSF). Differentiated BMM were harvested and frozen for subsequent experimentation. For treatment with compound C1089 (see Example 13), a frozen stock of Trex1-KO BMM was thawed and $1x10^5$ cells were plated in 96 well format. BMMs were treated with a dilution series of C1089 and incubated overnight at 37 ºC 5% CO_2, at which point cellular supernatants were harvested and stored at -80 ºC for subsequent analysis. The media used for this dilution series was without FBS. Remaining cells were evaluated for viability using Cell Titer Glo 2.0 kit according to the manufacturer instructions. BMM supernatants were evaluated for the secreted cytokine normal T cell expressed and secreted (RANTES/CCL5) or for secreted cytokine monocyte chemoattractant protein 1 (MCP-1/CCL2) using cytometric bead array mouse Flex Set kits (BD Biosciences). Cytokine concentration was calculated from a standard curve and normalized to vehicle (DMSO) treated cells.

[00504] Fig. 1 shows that C1089 can significantly inhibit cytokine secretion by diseased Trex1-KO BMM (RANTES/CCL5 IC_{50} = 1.251 μM, MCP-1/CCL2 IC_{50} = 6.973 μM). Additionally, BMM were 100% viable at these concentrations, indicating that inhibition is not simply due to cellular cytotoxicity. Additional compounds were assessed by this assay.

[00505] Table 17 below provides IC_{50} data for certain compounds of the invention for inhibition of RANTES expression. "A" indicates an IC_{50} value less than 5 μM, "B" indicates an IC_{50} value between 5 and 20 μM, and "C" indicates where an IC_{50} value could not be calculated from the data. ND indicates no data for that cytokine. In this table, column M refers to MCP-1 and column R refers to RANTES.

Table 17

Compound ID	BMM IC_{50} (μM)	
	M	R
A1052	C	ND
A1059	C	ND
A1082	C	C

Compound ID	BMM IC_{50} (μM)	
	M	R
A1095	C	C
A1129	B	C
A1134	A	A

Compound ID	BMM IC_{50} (μM)	
	M	R
A1139	C	C
C1008	C	ND
C1014	C	ND

Compound ID	BMM IC_{50} (μM)	
	M	R
C1029	C	C
C1045	C	B
C1047	B	A
C1053	C	C
C1055	C	C
C1056	C	ND
C1071	C	C
C1073	C	C
C1074	C	C
C1077	C	C
C1081	B	B
C1082	C	C
C1091	C	C
C1092	C	C
C1094	C	A
C1098	B	A
C1099	C	C
C1105	B	A
C1113	A	C
C1114	B	C
C1117	C	C
C1118	C	A
C1119	C	C
C1121	A	C
C1123	C	C
C1126	C	C
C1134	B	C
C1136	B	C

Compound ID	BMM IC_{50} (μM)	
	M	R
C1139	B	B
C1140	C	C
C1145	C	C
C1147	C	C
C1151	C	B
C1154	C	C
C1160	C	C
C1167	C	C
C1169	C	C
C1173	C	C
C1175	C	C
C1176	C	C
C1190	C	C
C1205	C	C
C1233	C	C
C1236	C	C
D1018	C	C
D1028	C	C
D1071	B	A

INCORPORATION BY REFERENCE

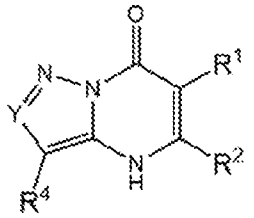
[00506] The disclosure of each of the patent documents and scientific articles referred to herein is incorporated by reference for all purposes.

EQUIVALENTS

[00507] The invention can be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting on the invention described herein. Scope of the invention is thus indicated by the appended claims rather than by the foregoing description, and all changes that come within the meaning and range of equivalency of the claims are intended to be embraced therein.

What is claimed is:

1. A compound of Formula (I):



(I),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, wherein

Y is $-CR^3=$ or $-N=$;

R^1 is Q^1-T^1-$(X^1)_n$;

Q^1 is a bond or C_{1-3}alkylene, wherein the C_{1-3}alkylene group is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w2}$, and $-NR^{w2}R^{x2}$;

T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, $-C(=O)C_{0-3}$alkylene-C_{3-8}cycloalkyl, $-C(=O)-C_{0-3}$alkylene-C_{6-10}aryl, $-C(=O)-C_{0-3}$alkylene-3 to 12-membered heterocycloalkyl, $-C(=O)-C_{0-3}$alkylene-5 to 10-membered heteroaryl, $-NR^aR^b$, $-S(=O)_2R^a$, $-NR^aC(=O)R^a$, $-NR^aC(=O)NR^aR^b$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^a$, $-C(=O)NR^aS(=O)_2R^a$, $-NR^aS(=O)_2NR^aR^b$, $-C(=O)NR^aR^b$, or $-S(=O)_2NR^aR^b$;

each X^1 is independently selected from the group consisting of halo, cyano, oxo, C_{0-3}alkylene-$C(=O)R^c$, C_{0-3}alkylene-OR^c, C_{0-3}alkylene-$C(=O)OR^c$, C_{0-3}alkylene-$OC(=O)R^c$, C_{0-3}alkylene-NR^cR^d, C_{0-3}alkylene-$N^+R^cR^dR^{d'}$, C_{0-3}alkylene-$S(=O)_mR^c$, C_{0-3}alkylene-$NR^cC(=O)R^c$, C_{0-3}alkylene-$NR^cC(=O)NR^cR^d$, C_{0-3}alkylene-$OC(=O)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=O)OR^c$, C_{0-3}alkylene-$NR^cS(=O)_2R^c$, C_{0-3}alkylene-$C(=O)NR^cS(=O)_2R^c$, C_{0-3}alkylene-$NR^cS(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=O)NR^cR^d$, C_{0-3}alkylene-$S(=O)_2NR^cR^d$, C_{0-3}alkylene-$C(=NR^c)NR^cR^d$, C_{0-3}alkylene-$NR^cC(=NR^c)NR^cR^d$, and R^{S1}, in which R^{S1} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S1} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, nitro, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-NR^eR^f, C_{0-3}alkylene-OR^e, C_{0-3}alkylene-$NR^eC(=O)R^e$, C_{0-3}alkylene-$NR^eC(=O)OR^e$, C_{0-3}alkylene-$NR^eC(=O)NR^eR^f$, C_{0-}

$_{3}$alkylene-OC(=O)R^e, C_{0-3}alkylene-C(=O)OR^e, C_{0-3}alkylene-C(=O)NR^eR^f, C_{0-3}alkylene-C(=O)R^e, C_{0-3}alkylene-S(=O)$_mR^e$, C_{0-3}alkylene-S(=O)$_2NR^eR^f$, C_{0-3}alkylene-$NR^eS(=O)_2R^e$, C_{0-3}alkylene-C(=O)$NR^eS(=O)_2R^e$, C_{0-3}alkylene-$NR^eS(=O)_2NR^eR^f$, and R^{S2}, in which R^{S2} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl,

and each R^{S2} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^w, and -NR^wR^x;

R^2 is Q^2-T^2-$(X^2)_p$;

Q^2 is a bond or C_{1-3}alkylene, wherein the C_{1-3}alkylene group is optionally substituted with one or more substituents independently selected from the group consisting of halo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w3}, and -$NR^{w3}R^{x3}$;

T^2 is H, halo, cyano, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, -C(=O)-C_{0-3}alkylene-C_{3-8}cycloalkyl, -C(=O)-C_{0-3}alkylene-C_{6-10}aryl, -C(=O)-C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, -C(=O)-C_{0-3}alkylene-5- to 10-membered heteroaryl, -OR^z, -S(=O)$_mR^k$, -P(=O)$R^{kk}R^{mm}$, -NR^kR^m, -C(=O)OR^k, or -C(=O)NR^kR^m;

each X^2 is independently selected from the group consisting of halo, cyano, oxo, C_{0-3}alkylene-OR^n, C_{0-3}alkylene-S(=O)$_mR^n$, C_{0-3}alkylene-NR^nR^o, C_{0-3}alkylene-C(=O)NR^nR^o, C_{0-3}alkylene-C(=O)OR^n, and R^{S3}, in which R^{S3} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and R^{S3} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^p, C_{0-3}alkylene-S(=O)$_mR^p$, C_{0-3}alkylene-NR^pR^q, C_{0-3}alkylene-C(=O)NR^pR^q, C_{0-3}alkylene-C_{0-3}alkylene-C(=O)OR^p, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S4}, in which R^{S4} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S4} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w4}, and -$NR^{w4}R^{x4}$;

R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{3-6}cycloalkyl, -CN, -OR^r, -C(=O)R^r, -S(=O)$_mR^r$, NR^rR^t, or -C(=O)OR^r, wherein C_{1-3}alkyl, C_{2-3}alkenyl and C_{2-3}alkynyl

are optionally substituted with one C_{3-6}cycloalkyl;

R^4 is C_{1-6}alkyl, C_{1-6}haloalkyl, $S(=O)_mR^u$, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl, wherein C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, OR^{w5}, and $NR^{w5}R^{x5}$;

each of R^a and R^b, independently, is H or R^{S5}, in which R^{S5} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and R^{S5} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}haloalkyl, C_{0-3}alkylene-OR^{c2}, C_{0-3}alkylene-$C(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)OR^{c2}$, C_{0-3}alkylene-$OC(=O)R^{c2}$, C_{0-3}alkylene-$C(=O)NR^{c2}R^{d2}$, C_{0-3}alkylene-$S(=O)_mR^{c2}$, C_{0-3}alkylene-$S(=O)_2NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}C(=O)R^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)OR^{c2}$, C_{0-3}alkylene-$NR^{c2}C(=O)NR^{c2}R^{d2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$C(=O)NR^{c2}S(=O)_2R^{c2}$, C_{0-3}alkylene-$NR^{c2}S(=O)_2NR^{c2}R^{d2}$, C_{0-3}alkylene-$N(S(=O)_2R^{c2})_2$, and R^{S6}, in which R^{S6} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S6} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{e2}R^{f2}$, C_{0-3}alkylene-OR^{e2}, C_{0-3}alkylene-$NR^{e2}C(=O)R^{e2}$, C_{0-3}alkylene-$NR^{e2}C(=O)OR^{e2}$, C_{0-3}alkylene-$NR^{e2}C(=O)NR^{e2}R^{f2}$, C_{0-3}alkylene-$OC(=O)R^{e2}$, C_{0-3}alkylene-$C(=O)OR^{e2}$, C_{0-3}alkylene-$C(=O)NR^{e2}R^{f2}$, C_{0-3}alkylene-$C(=O)R^{e2}$, C_{0-3}alkylene-$S(=O)_mR^{e2}$, C_{0-3}alkylene-$S(=O)_2NR^{e2}R^{f2}$, C_{0-3}alkylene-$NR^{e2}S(=O)_2R^{e2}$, C_{0-3}alkylene-$C(=O)NR^{e2}S(=O)_2R^{e2}$, C_{0-3}alkylene-$NR^{e2}S(=O)_2NR^{e2}R^{f2}$, and R^{S7}, in which R^{S7} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S7} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w6}$, and $-NR^{w6}R^{x6}$;

each of R^c, R^{c2}, R^d, $R^{d'}$, and R^{d2}, independently, is H or R^{S8}, in which R^{S8} is C_{1-6}alkyl,

C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S8} is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{e3}R^{f3}$, C_{0-3}alkylene-OR^{e3}, C_{0-3}alkylene-$C(=O)OR^{e3}$, C_{0-3}alkylene-$C(=O)NR^{e3}R^{f3}$, C_{0-3}alkylene-$C(=O)R^{e3}$, C_{0-3}alkylene-$S(=O)_mR^{e3}$, C_{0-3}alkylene-$S(=O)_2NR^{e3}R^{f3}$, C_{0-3}alkylene-$NR^{f3}C(=O)R^{e3}$, C_{0-3}alkylene-$NR^{f3}S(=O)_mR^{e3}$, and R^{S9}, in which R^{S9} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S9} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w7}$, and $-NR^{w7}R^{x7}$;

each of R^e, R^{e2}, R^{e3}, R^f, R^{f2}, and R^{f3}, independently, is H or R^{S10}, in which R^{S10} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S10} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, $-OR^{w8}$, and $-NR^{w8}R^{x8}$;

each of R^{kk}, and R^{mm}, is independently selected from the group consisting of R^k, $-OR^k$, and $-NR^kR^m$;

each of R^k, and R^m, independently, is H or R^z, in which R^z is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^z is optionally substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{0-3}alkylene-$NR^{n2}R^{o2}$, C_{0-3}alkylene-OR^{n2}, C_{0-3}alkylene-$C(=O)OR^{n2}$, C_{0-3}alkylene-$C(=O)NR^{n2}R^{o2}$, C_{0-3}alkylene-$C(=O)R^{n2}$, C_{0-3}alkylene-$S(=O)_mR^{n2}$, C_{0-3}alkylene-$S(=O)_2NR^{n2}R^{o2}$, and R^{S11}, in which R^{S11} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S11} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p2}, C_{0-3}alkylene-$S(=O)_mR^{p2}$, C_{0-3}alkylene-$NR^{p2}R^{q2}$, C_{0-3}alkylene-$C(=O)NR^{p2}R^{q2}$,

C_{0-3}alkylene-C_{0-3}alkylene-C(=O)OR^{p2}, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S12}, in which R^{S12} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S12} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w9}, and -$NR^{w9}R^{x9}$;

each of R^{n}, R^{n2}, R^{o}, and R^{o2}, independently, is H or R^{S13}, in which R^{S13} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S13} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, cyano, C_{0-3}alkylene-OR^{p3}, C_{0-3}alkylene-$S(=O)_mR^{p3}$, C_{0-3}alkylene-$NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)NR^{p3}R^{q3}$, C_{0-3}alkylene-$C(=O)OR^{p3}$, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, and R^{S14}, in which R^{S14} is C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S14} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w10}, and -$NR^{w10}R^{x10}$;

each of R^{p}, R^{p2}, R^{p3}, R^{q}, R^{q2}, and R^{q3}, independently, is H or R^{S15}, in which R^{S15} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

each R^{S15} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w11}, and -$NR^{w11}R^{x11}$;

each of R^{r}, R^{t}, and R^{u}, independently, is H or R^{S16}, in which R^{S16} is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-3}alkylene-C_{3-8}cycloalkyl, C_{0-3}alkylene-C_{6-10}aryl, C_{0-3}alkylene-3- to 12-membered heterocycloalkyl, or C_{0-3}alkylene-5- to 10-membered heteroaryl;

and each R^{S16} is optionally substituted with one or more substituents independently selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -C(=O)OR^{w12}, -OR^{w12}, and -$NR^{w12}R^{x12}$;

each R^{w}, R^{w2}, R^{w3}, R^{w4}, R^{w5}, R^{w6}, R^{w7}, R^{w8}, R^{w9}, R^{w10}, R^{w11}, R^{w12}, R^{x}, R^{x2}, R^{x3}, R^{x4}, R^{x5}, R^{x6}, R^{x7}, R^{x8}, R^{x9}, R^{x10}, R^{x11}, and R^{x12}, independently, is H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}haloalkyl;

each of n and p independently is 0, 1, 2, 3, 4, or 5, wherein when T^2 is H, p is 0; and m is 0, 1, or 2;

with the proviso that, for compounds where Y is $-CR^3=$:

a) when R^1 is unsubstituted phenyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl, unsubstituted phenyl, or unsubstituted pyridine;

b) when R^1 is unsubstituted cyclohexyl, R^2 is methyl and R^3 is methyl, R^4 is not unsubstituted pyridine;

c) when R^1 is unsubstituted cyclopentyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl or unsubstituted pyridine,

d) when R^2 is methyl, R^3 is methyl and R^4 is 3,4-di-ethoxy-phenyl, R^1 is not unsubstituted 1-pyrrolidine, unsubstituted 1-piperidine, 4-methyl-1-piperidine, 4-(phenylmethyl)-1-piperidine, unsubstituted 2-1,2,3,4-tetrahydro-isoquinoline, unsubstituted morpholine, or $NHCH_2CH_2$-3-indole;

e) when R^1 is unsubstituted CH_2-phenyl, R^2 is methyl and R^3 is methyl, R^4 is not ethyl, trifluoromethyl, 1-methyl-piperidin-4-yl, unsubstituted pyridine, unsubstituted phenyl, phenyl mono-substituted with 4-F, 4-Cl, 2-methoxy or 4-methoxy, or phenyl disubstituted with 3,4-methoxy;

f) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted pyridine, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 4-CN, 4-NO_2, 4-F or 2-F;

g) when R^2 is methyl, R^3 is methyl and R^4 is ethyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 4-CN or 4-NO_2;

h) when R^2 is methyl, R^3 is methyl and R^4 is 4-methoxy-phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 3-Cl, 4-Br, 2-methyl or 4-methyl;

i) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 3-Cl, 4-Cl, 4-Br, 2-methyl, 3-methyl, 4-methyl, 4-isopropyl or 4-*tert*-butyl; or R^1 is not unsubstituted CH_2-1-naphthylene or unsubstituted CH_2-pyridine;

j) when R^2 is methyl, R^3 is methyl and R^4 is 4-Cl-phenyl, R^1 is not CH_2-phenyl wherein the phenyl is substituted with 2-Cl, 4-Cl or 4-isopropyl;

k) when R^1 is unsubstituted CH_2-phenyl, R^2 is methyl and R^3 is trifluoromethyl, R^4 is not unsubstituted phenyl or phenyl substituted with 2-Cl or 4-Cl;

l) the compound is not wherein R^1 is CH_2-4-Br-phenyl, R^2 is methyl, R^3 is ethyl and R^4 is unsubstituted phenyl;

m) when R^2 is methyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not

$CH_2CH_2C(=O)NH$-phenyl wherein the phenyl ring is unsubstituted or is substituted at the 4-position with Cl, methyl or methoxy;

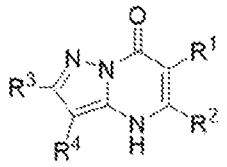
n) when R^2 is methyl or ethyl, R^3 is methyl and R^4 is unsubstituted phenyl, R^1 is not substituted pyrazolo[1,5-*a*]pyrimidin-7-yl;

o) when R^2 is H, R^3 is isopropyl and R^4 is methyl, R^1 is not unsubstituted pyrazole; and

p) the compound is not wherein R^1 is unsubstituted CH_2-phenyl, R^2 is H, R^3 is methyl and R^4 is unsubstituted phenyl; and

with the proviso that, for compounds where Y is -N=, the compound is not wherein R^1 is unsubstituted phenyl, R^2 is H and R^4 is 2-fluoro-phenyl.

2. The compound of claim 1, wherein the compound is of Formula (IA):


(IA),

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

3. The compound of claim 1 or 2, wherein Q^1 is a bond and T^1 is C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, and n is 0, 1, 2, 3 or 4.

4. The compound of claim 1 or 2, wherein Q^1 is a bond or $-CH_2-$ and T^1 is C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, 5- to 10-membered heteroaryl, or $-C(=O)NR^aR^b$.

5. The compound of claim 1 or 2, wherein Q^1 is a bond or $-CH_2-$, T^1 is $-C(=O)NR^aR^b$ and n is 0.

6. The compound of any one of claims 1-4, wherein T^1 is 9- or 10-membered bicyclic heteroaryl.

7. The compound of any one of claims 1, 2, 4 and 5, wherein one of R^a and R^b is H or methyl.

8. The compound of any one of claims 1, 2, 4 and 5, wherein one of R^a and R^b independently is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indazolyl, benzimidazolyl, imidazopyridinyl, quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, oxadiazolyl, triazolyl, imidazolyl, furan, or thiophenyl, and the other is hydrogen or methyl.

9. The compound of any one of claims 1-8, wherein R^2 is Q^2-T^2-$(X^2)_p$, Q^2 is a bond, T^2 is H, halo, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, or C_{2-6}alkynyl, and each X^2 independently is halo or -OC_{1-6}alkyl.

10. The compound of any one of claims 1-8, wherein R^2 is H, cyano, methyl or methoxymethyl.

11. The compound of any one of claims 1-10, wherein R^3 is C_{1-3}alkyl, C_{1-3}haloalkyl, -CN, -S(=O)$_2C_{1-3}$alkyl or -C(=O)OC_{1-3}alkyl.

12. The compound of any one of claims 1-10, wherein R^3 is -CN, C_{1-3}alkyl, C_{1-3}haloalkyl or -C(=O)OC_{1-3}alkyl.

13. The compound of any one of claims 1-10, wherein R^3 is -CN or $-CF_3$.

14. The compound of any one of claims 1-13, wherein R^4 is C_{1-3}alkyl, C_{1-3}haloalkyl, -S(=O)$_2C_{1-3}$alkyl, C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl, wherein C_{3-8}cycloalkyl, C_{6-10}aryl, 3- to 12-membered heterocycloalkyl, or 5- to 10-membered heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$.

15. The compound of any one of claims 1-13, wherein R^4 is C_{3-8}cycloalkyl or C_{6-10}aryl, wherein C_{3-8}cycloalkyl and C_{6-10}aryl are optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

16. The compound of any one of claims 1-13, wherein R^4 is phenyl optionally substituted with 1-3 substituents selected from the group consisting of halo, oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyano, C_{1-6}haloalkyl, -OR^{w5}, and -$NR^{w5}R^{x5}$, wherein R^{w5} and R^{x5} are independently H, C_{1-6}alkyl or C_{1-6}haloalkyl.

17. The compound of any one of claims 1-4 and 9-16, wherein T^1 is aryl or heteroaryl.

18. The compound of any one of claims 1-4 and 9-16, wherein T^1 is 5- or 6-membered monocyclic heteroaryl or 9- or 10-membered bicyclic heteroaryl.

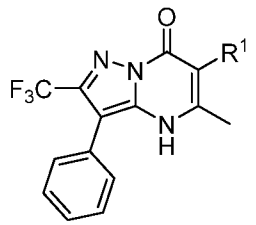
19. The compound of any one of claims 1-4 and 9-16, wherein T^1 is pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, indolyl, indolinyl, isoindolyl, isoindolinyl, indazolyl, pyrazolopyridinyl, pyrazolopyrimidinyl, oxazolopyrimidinyl, oxazolopyridinyl, imidazopyridinyl, benzimidazolyl, tetrahydrobenzimidazolyl, benzofuranyl, dihydrobenzofuranyl, isobenzofuranyl, dihydroisobenzofuranyl, triazolopyridinyl, benzothiazolyl, azabenzimidazolyl, azabenzoxazolyl, azabenzothiazolyl, imidazopyridinyl,

quinolinyl, isoquinolinyl, quinazolinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzoxazolyl, benzodioxolyl, chromanyl, tetrahydrooxazoloazepinyl, tetrahydrobenzoxazolyl, oxadiazolyl, thiadiazolyl, pyrazolyl, triazolyl, imidazolyl, furanyl, or thiophenyl.

20. The compound of any one of claims 1-4 and 9-16, wherein T^1 is 3- to 12-membered heterocycloalkyl.

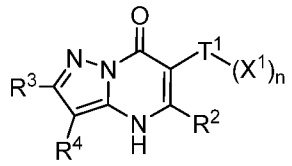
21. The compound of claim 20, wherein T^1 is piperazine, piperidine, quinuclidine, or morpholine.

22. The compound of claim 1 or 2, wherein the compound is of Formula (Ib):



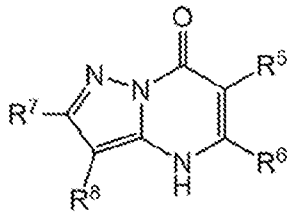
(Ib).

23. The compound of claim 1 or 2, wherein the compound is of Formula (IIa):



(IIa).

24. A compound of Formula (III):



(III),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, wherein

R^5 is selected from the group consisting of $-C(=O)NR^9R^{10}$; $-CH_2C(=O)NR^{11}R^{12}$; $-CH_2CH_2NR^{13}R^{14}$; $-CH_2$-phenyl; $-CH_2$-5-membered monocyclic heteroaryl optionally substituted with one C_{1-3}alkyl, monocyclic C_{5-6}cycloalkyl, or phenyl, wherein phenyl is optionally substituted with one $-OC_{1-3}$alkyl; phenyl optionally substituted with one halo or C_{1-3}alkyl; a 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with 1, 2, or 3 R^{15}; a 5- or 6-membered monocylic heteroaryl optionally substituted with 1, 2, or 3 R^{16}; and 9- or 10-membered bicyclic heteroaryl optionally substituted with 1, 2, 3, or 4 R^{17};

R^9 and R^{10} are independently selected from the group consisting of H; C_{1-3}alkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH and -OC_{1-3}alkyl; -CH_2phenyl; -$S(=O)_2R^{18}$; C_{5-6}cycloalkyl optionally substituted with one -NH_2, oxo, -OH, or -OC_{1-3}alkyl; phenyl optionally substituted with 1, 2, or 3 R^{19}; a 5-or 6-membered monocyclic heterocycloalkyl optionally substituted with one -C_{1-3}alkyl, -$C(=O)C_{1-3}$alkyl, or -$C(=O)OC_{1-6}$alkyl; a 5- or 6-membered monocyclic heteroaryl optionally substituted with 1, 2, or 3 R^{20}; and a 9- or 10-membered bicyclic heteroaryl optionally substituted with 1 or 2 halo; or

R^9 and R^{10} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one phenyl;

R^{11} and R^{12} are independently selected from the group consisting of H; C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl; phenyl optionally substituted with one -NH_2 or -OC_{1-3}alkyl; and a 5- or 6-membered monocyclic heteroaryl; or R^{11} and R^{12} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one C_{1-3}alkyl, phenyl or -CH_2-phenyl, wherein the phenyl ring of phenyl or -CH_2-phenyl is optionally substituted with one C_{1-3}alkyl;

R^{13} and R^{14} are independently selected from the group consisting of H; -$C(=O)C_{1-3}$alkyl; -C(=O)phenyl; and phenyl optionally substituted with one -OC_{1-3}alkyl;

each R^{15} is independently selected from the group consisting of oxo; -C(=O)OH; -$C(=O)OC_{1-3}$alkyl; and C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl;

each R^{16} is independently selected from the group consisting of -CN; -C(=O)OH; -$C(=O)OC_{1-3}$alkyl; -$C(=O)NH_2$; -$C(=O)NHC_{1-3}$alkyl; -$C(=O)N(C_{1-3}alkyl)_2$; -$C(=NH)NH_2$; -$NHC(=NH)NH_2$; -NH_2; -NHC_{1-3}alkyl;-$N(C_{1-3}alkyl)_2$; -NHC_{3-6}cycoalkyl; -$N(C_{1-3}alkyl)C_{3-6}$cycloalkyl; C_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, or 5- or 6-membered monocyclic heterocycloalkyl, wherein the monocyclic heterocycloalkyl is optionally substituted with -C_{1-3}alkyl; C_{1-3}haloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH and phenyl; -C_{3-6}cycloalkyl optionally substituted with one -NH_2, C_{1-3}alkyl, C_{1-3}haloalkyl, or -OC_{1-3}alkyl; phenyl optionally substituted with one -OH, -OC_{1-3}alkyl, -NO_2, -NH_2, -NHC_{1-3}alkyl, or -$N(C_{1-3}alkyl)_2$; 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of oxo, -OH, -NH_2, -OC_{1-3}alkyl,

-C(=O)C_{1-3}alkyl, -S(=O)$_2C_{1-3}$alkyl, -C(=O)OC_{1-6}alkyl, -C(=O)OCH_2phenyl, and C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -NH_2, -NHS(=O)$_2C_{1-3}$alkyl, -OH, or -OC_{1-3}alkyl; and 5- or 6-membered monocyclic heteroaryl optionally substituted with one -OH or -OC_{1-3}alkyl;

each R^{17} is independently selected from the group consisting of oxo; halo; -OH; -CN; -NH_2; -NHC_{1-3}alkyl; -N(C_{1-3}alkyl)$_2$; -N^+(C_{1-3}alkyl)$_3$; -NHC(=O)C_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -S(=O)$_m$$C_{1-3}$alkyl; -C(=O)OH; -C(=O)O$C_{1-6}$alkyl; -C(=O)$NH_2$; -C(=O)NH$C_{1-3}$alkyl; -C(=O)N($C_{1-3}$alkyl)$_2$; -OC(=O)$NH_2$; -OC(=O)NH$C_{1-3}$alkyl; -OC(=O)N($C_{1-3}$alkyl)$_2$; -C(=NH)$NH_2$; -C(=NH)NH$C_{1-3}$alkyl; -C(=NH)N($C_{1-3}$alkyl)$_2$; -O$C_{1-3}$haloalkyl; C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; -OC_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, phenyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -C(=O)NH_2, -C(=O)NHC_{1-3}alkyl, -C(=O)N(C_{1-3}alkyl)$_2$, -NH_2, -NHC_{1-3}alkyl, -N(C_{1-3}alkyl)$_2$, -NHC(=O)C_{1-3}alkyl, or -NHS(=O)$_2C_{1-3}$alkyl; and phenyl optionally substituted with one halo, -CN, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl or -N(C_{1-3}alkyl)$_2$;

R^{18} is selected from the group consisting of C_{1-3}alkyl; monocyclic C_{3-6}cycloalkyl; a 5- or 6-membered monocyclic heteroaryl; phenyl; and -CH_2phenyl; wherein the phenyl ring of phenyl or -CH_2phenyl is optionally substituted with one halo, -CN, or -OC_{1-3}alkyl;

each R^{19} is independently selected from the group consisting of halo; -CN; -NH_2; -NHC_{1-3}alkyl; -N(C_{1-3}alkyl)$_2$; -NHC(=O)C_{1-3}alkyl; -NHS(=O)$_2C_{1-3}$alkyl; -N(S(=O)$_2C_{1-3}$alkyl)$_2$;-NHS(=O)$_2C_{3-6}$cycloalkyl; -NHS(=O)$_2$phenyl; -NHC(=O)OH; -NHC(=O)OC_{1-3}alkyl; -S(=O)$_2C_{1-3}$alkyl; -OC_{1-3}alkyl optionally substituted with one phenyl; C_{1-3}haloalkyl; -OC_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; a 5- or 6-membered monocyclic heterocycloalkyl; and C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$;

each R^{20} is independently selected from the group consisting of -CN; -OC_{1-3}alkyl; -S(=O)$_2C_{1-3}$alkyl; C_{1-3}haloalkyl; and C_{1-3}alkyl optionally substituted with one -OH or -OC_{1-3}alkyl; and monocyclic C_{3-6}cycloalkyl;

R^6 is selected from the group consisting of H; halo; -CN; -NH_2; -C(=O)OH; -C(=O)OC_{1-3}alkyl; -C(=O)C_{1-3}alkyl; -S(=O)$_m$$C_{1-3}$alkyl; -P(=O)($C_{1-3}$alkyl)$_2$; -C(=O)$NR^{21}R^{22}$; C_{1-3}haloalkyl; -OC_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; C_{1-3}alkyl optionally substituted with one -NH_2,

-NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)_2$, -C(=O)OH, -$C(=O)OC_{1-3}$alkyl, -$S(=O)_mC_{1-3}$alkyl, -$C(=O)C_{1-3}$alkyl, -OR^{23}, or 5- or 6-membered monocyclic heteroaryl, wherein monocyclic heteroaryl is optionally substituted with 1 or 2 C_{1-3}alkyl; monocyclic C_{3-6}cycloalkyl optionally substituted with one -C(=O)OH, -$C(=O)OC_{1-3}$alkyl or C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -OH or -OC_{1-3}alkyl; a 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one -C(=O)OH, or -$C(=O)OC_{1-3}$alkyl; and a 5- or 6-membered heteroaryl optionally substituted with 1 or 2 C_{1-3}alkyl;

R^{21} and R^{22} are independently selected from the group consisting of H; C_{1-6}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, -$C(=O)OC_{1-3}$alkyl, -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)_2$, or 5- or 6-membered monocyclic heteroaryl; C_{1-3}haloalkyl optionally substituted with one -OH or -OC_{1-3}alkyl; a 5- or 6-membered monocyclic heteroaryl optionally substituted with 1 or 2 C_{1-3}alkyl; and a 4- to 6-membered monocyclic heterocycloalkyl; or

R^{21} and R^{22} combine with the nitrogen to which they are bound to form an N-linked 5- or 6-membered monocyclic heterocycloalkyl optionally substituted with one -C(=O)OH, -$C(=O)OC_{1-3}$alkyl, or C_{1-3}alkyl, wherein C_{1-3}alkyl is optionally substituted with one -OH or -OC_{1-3}alkyl;

R^{23} is selected from the group consisting of H; C_{1-3}haloalkyl; C_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, -$C(=O)OC_{1-3}$alkyl, -$C(=O)NH_2$, -$C(=O)NHC_{1-3}$alkyl, -$C(=O)N(C_{1-3}alkyl)_2$, phenyl, 5- or 6-membered monocyclic heteroaryl, or 5- or 6-membered monocyclic heterocycloalkyl, wherein monocyclic heterocycloalkyl is optionally substituted with 1 or 2 oxo or C_{1-3}alkyl; a 4-, 5-, or 6-membered monocyclic heterocycloalkyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of oxo and C_{1-3}alkyl; and a 5- or 6-membered monocyclic heteroaryl;

R^7 is selected from the group consisting of -CN; -OH; -C(=O)OH; -$C(=O)OC_{1-3}$alkyl; -$C(=O)C_{1-3}$alkyl; -$S(=O)_mC_{1-3}$alkyl; -NH_2; -NHC_{1-3}alkyl; -$N(C_{1-3}alkyl)_2$; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl; C_{1-3}haloalkyl; C_{2-3}alkenyl optionally substituted with one monocyclic C_{3-6}cycloalkyl; C_{2-3}alkyny optionally substituted with one monocyclic C_{3-6}cycloalkyl; monocyclic C_{3-6}cycloalkyl; -O-5- or 6-membered monocyclic heterocycloalkyl; and -OC_{1-3}alkyl optionally substituted with one -OH, -OC_{1-3}alkyl, -C(=O)OH, or -$C(=O)OC_{1-3}$alkyl; and

R^8 is selected from the group consisting of C_{1-3}alkyl; C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; phenyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of -CN, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl

and -OC_{1-3}haloalkyl; and pyridinyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of -CN, halo, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl and -OC_{1-3}haloalkyl,

with the proviso that:

a) when R^5 is unsubstituted phenyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl, unsubstituted phenyl, or unsubstituted pyridine;

b) when R^5 is unsubstituted cyclohexyl, R^6 is methyl and R^7 is methyl, R^8 is not unsubstituted pyridine;

c) when R^5 is unsubstituted cyclopentyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl or unsubstituted pyridine,

d) when R^6 is methyl, R^7 is methyl and R^8 is 3,4-di-ethoxy-phenyl, R^5 is not unsubstituted 1-pyrrolidine, unsubstituted 1-piperidine, 4-methyl-1-piperidine, unsubstituted 2-1,2,3,4-tetrahydro-isoquinoline, or unsubstituted morpholine;

e) when R^5 is unsubstituted CH_2-phenyl, R^6 is methyl and R^7 is methyl, R^8 is not ethyl, trifluoromethyl, unsubstituted pyridine, unsubstituted phenyl, phenyl mono-substituted with 4-F, 4-Cl, 2-methoxy or 4-methoxy, or phenyl disubstituted with 3,4-methoxy;

f) when R^5 is unsubstituted CH_2-phenyl, R^6 is methyl and R^7 is trifluoromethyl, R^8 is not unsubstituted phenyl or phenyl substituted with 2-Cl or 4-Cl;

g) when R^6 is methyl, R^7 is methyl and R^8 is unsubstituted phenyl, R^5 is not $CH_2CH_2C(=O)NH$-phenyl wherein the phenyl ring is unsubstituted or is substituted at the 4-position with Cl, methyl or methoxy;

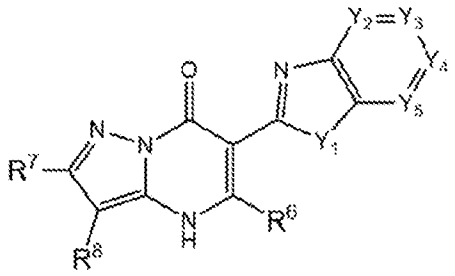
h) when R^6 is methyl or ethyl, R^7 is methyl and R^8 is unsubstituted phenyl, R^5 is not substituted pyrazolo[1,5-*a*]pyrimidin-7-yl;

i) when R^6 is H, R^7 is isopropyl and R^8 is methyl, R^5 is not unsubstituted pyrazole; and

j) the compound is not wherein R^5 is unsubstituted CH_2-phenyl, R^6 is H, R^7 is methyl and R^8 is unsubstituted phenyl.

25. The compound of claim 24, wherein R^5 is a 9- or 10-membered bicyclic heteroaryl optionally substituted with 1, 2, 3, or 4 R^{17}.

26. The compound of claim 24, wherein the compound is of Formula (IIIa):



(IIIa),

or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, wherein Y_1 is -O-, -NH-, -NR^{24}-, or -S-, and Y_2, Y_3, Y_4, and Y_5 are -N= or -CR^{25}=, provided that 0, 1 or 2 of Y_2, Y_3, Y_4, and Y_5 are -N=; wherein R^{24} is selected from the group consisting of C_{1-3}haloalkyl; monocyclic C_{3-6}cycloalkyl; C_{1-3}alkyl optionally substituted with one monocyclic C_{3-6}cycloalkyl, -OH, -OC_{1-3}alkyl, -C(=O)OH, -C(=O)OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl, or -N(C_{1-3}alkyl)$_2$; and phenyl optionally substituted with one halo, -CN, C_{1-3}alkyl, C_{1-3}haloalkyl, -OC_{1-3}alkyl, -NH_2, -NHC_{1-3}alkyl or -N(C_{1-3}alkyl)$_2$; and wherein R^{25} is H or R^{17}, provided that 0, 1, 2 or 3 of Y_2, Y_3, Y_4, and Y_5 are -CR^{25}= wherein R^{25} is R^{17}.

27. The compound of claim 1, wherein the compound is selected from the group consisting of a compound as recited in Table 1A or Table 1B.

28. A pharmaceutical composition comprising the compound of any one of the preceding claims, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, together with a pharmaceutically acceptable diluent or carrier.

29. A method of inhibiting the cGAS/STING pathway in a cell, comprising contacting the cell with the compound of any one of claims 1 to 27, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, or the composition of claim 28.

30. A method of inhibiting cytokine production in a cell, comprising contacting the cell with the compound of any one of claims 1 to 27, or pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, or the composition of claim 28.

31. A method of treating a cGAS/STING pathway-mediated condition, comprising administering to a subject in need thereof an effective amount of a compound of any one of

claims 1 to 27, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, or the composition of claim 28.

32. The method of claim 31, wherein the cGAS/STING pathway-mediated condition is an autoimmune, inflammatory, or neurodegenerative condition.

33. A method of treating a disease in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of the compound of any one of claims 1 to 27, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, or the composition of claim 28, wherein the disease is selected from the group consisting of systemic inflammatory response syndrome (SIRS), sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature) syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis, vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease.

34. A method of treating a disease in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of the compound of any one of claims 1 to 27, including any pharmaceutically acceptable salt, pharmaceutically acceptable solvate or pharmaceutically acceptable hydrate thereof, or the composition of claim 28, in combination with a Janus Kinase (Jak) inhibitor, wherein the disease is selected from the group consisting of systemic inflammatory response syndrome (SIRS), sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature) syndrome, chilblain

lupus erythematosus, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis, vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease.

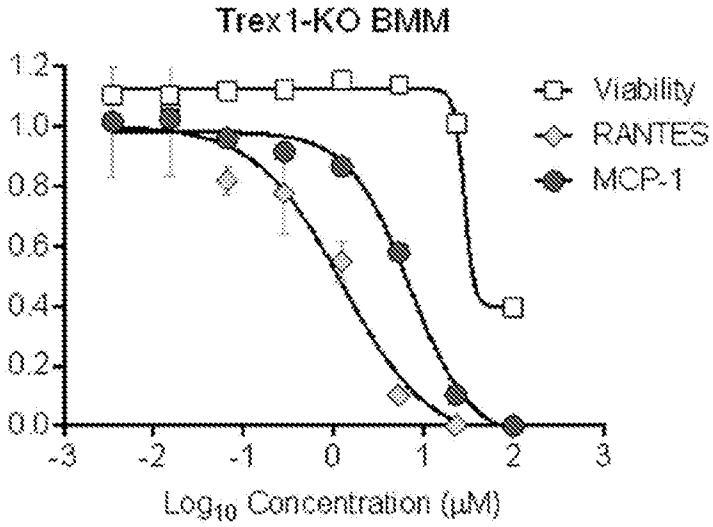
35. A compound of any one of claims 1 to 27, for use in the treatment of a cGAS/STING pathway-mediated condition.

36. A compound of any one of claims 1 to 27, for use in combination with a Janus Kinase inhibitor, for the treatment of a disease selected from the group consisting of systemic inflammatory response syndrome (SIRS), sepsis, septic shock, atherosclerosis, celiac disease, dermatomyositis, scleroderma, interstitial cystitis, transplant rejection (e.g. graft-versus-host disease), Aicardi-Goutieres Syndrome, Hutchison Guilford progeria syndrome, Singleton-Merten Syndrome, proteasome-associated autoinflammatory syndrome, SAVI (STING-associated vasculopathy with onset in infancy), CANDLE (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature) syndrome, chilblain lupus erythematosus, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, Wegener's disease, inflammatory bowel disease (*e.g.* ulcerative colitis, Crohn's disease), idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, glomerulonephritis, autoimmune myocarditis, myasthenia gravis, vasculitis, Type 1 diabetes, Type 2 diabetes, Sjorgen's syndrome, X-linked reticulate pigmentary disorder, polymyositis, spondyloenchondrodysplasia, age-related macular degeneration, Alzheimer's disease and Parkinson's disease.

37. Composition comprising a compound of any one of claims 1 to 27 and a Janus Kinase inhibitor.

38. A kit comprising a compound of any one of claims 1 to 27 and a Janus Kinase inhibitor.

FIG. 1


Trex1-KO BMM
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-3
-2
-1
0
1
2
3
Log10 Concentration (μM)
Viability
RANTES
MCP-1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/051014

A. CLASSIFICATION OF SUBJECT MATTER

C07D 487/04(2006.01)i, C07D 498/04(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D 487/04; A61K 31/44; A61K 31/517; A61K 31/519; A61K 31/55; A61K 45/06; C07D 471/04; C07D 498/02; C07D 498/04

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(Kipo internal), STN (Registry, Caplus, Marpat) & Keywords: pyrazolpyrimidinone, cGAS/STING pathway, Jak inhibitor

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2015-0065522 A1 (GENENTECH, INC. et al.) 05 March 2015 See paragraphs [0048], [0144]; and claims 1, 8.	1-5,22-27
X	WO 2017-069279 A1 (TAKEDA PHARMACEUTICAL COMPANY LIMITED) 27 April 2017 See abstract; and compound 84 (page 233) etc.	1-4,22-27
X	US 2014-0163033 A1 (FRANCISCO JAVIER BERNAL ANCHUELA et al.) 12 June 2014 See claims 1, 22-25.	1-4,22-27
X	US 8426595 B2 (HUANG, X. et al.) 23 April 2013 See abstract; and claims 1-8.	1,2,4,22-24
A	WO 2009-076593 A1 (VERTEX PHARMACEUTICALS INCORPORATED et al.) 18 June 2009 See the whole document.	1-5,22-27
A	JP 2005-008581 A (KISSEI PHARMACEUT CO., LTD.) 13 January 2005 See claims 1-17.	1-5,22-27

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
09 January 2019 (09.01.2019)	**09 January 2019 (09.01.2019)**

Name and mailing address of the ISA/KR
International Application Division
Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon, 35208, Republic of Korea
Facsimile No. +82-42-481-8578

Authorized officer
KAM, Yoo Lim
Telephone No. +82-42-481-3516

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2018/051014

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2018/051014

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JP 2005-008581 A	13/01/2005	None	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/051014

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 29-34
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 29-34 pertain to a method for treating a human body, and thus relate to a subject matter not required to search under PCT Article 17(2)(a)(i) and Rule 39.1(iv).

2. ☒ Claims Nos.: 21, 32
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claims 21 and 32 refer to the multiple dependent claim which does not comply with PCT Rule 6.4(a).

3. ☒ Claims Nos.: 6-20, 28-31, 33-38
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required addtional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.