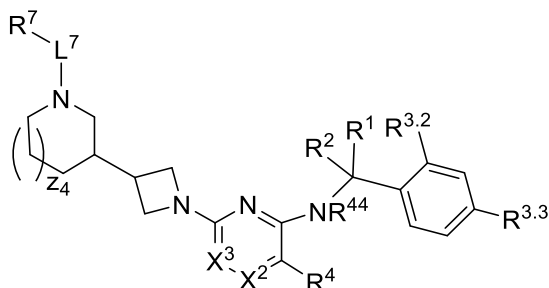


1. A compound having structural Formula (II):



acceptable salt thereof, wherein:

X^3 is CR^{10} or N :

n1, n2, n3.2, n3.3, n4, n7, n9, n10, and n44 are independently an integer from 0 to 4;

$m_1, m_2, m_{3.2}, m_{3.3}, m_4, m_7, , m_9, m_{10}, v_1, v_2, v_{3.2}, v_{3.3}, v_4, v_7, , v_9, v_{10}$,
and v_{44} are independently 1 or 2:

z4 is an integer from 0 to 2;

L⁷ is a bond, -O-, -S-, -NR^{7.2B}-, -C(O)-, -C(O)O-, -S(O)-, -S(O)₂-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R¹ is hydrogen, halogen, -CX^{1.1}₃, -CHX^{1.1}₂, -CH₂X^{1.1}, -CN, -N₃, -SO_{n1}R^{1A}, -SO_{v1}NR^{1B}R^{1C}, -NHN^{1B}R^{1C}, -ONR^{1B}R^{1C}, -NHC(O)NHN^{1B}R^{1C}, -NHC(O)NR^{1B}R^{1C}, -N(O)_{m1}, -NR^{1B}R^{1C}, -C(O)R^{1D}, -C(O)OR^{1D}, -C(O)NR^{1B}R^{1C}, -OR^{1A}, -NR^{1B}SO₂R^{1A}, -NR^{1B}C(O)R^{1D}, -NR^{1B}C(O)OR^{1D}, -NR^{1B}OR^{1D}, -OCX^{1.1}₃, -OCHX^{1.1}₂, -OCH₂X^{1.1}, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R² is hydrogen, halogen, -CX^{2.1}₃, -CHX^{2.1}₂, -CH₂X^{2.1}, -CN, -N₃, -SO_{n2}R^{2A}, -SO_{v2}NR^{2B}R^{2C}, -NHN^{2B}R^{2C}, -ONR^{2B}R^{2C}, -NHC(O)NHN^{2B}R^{2C}, -NHC(O)NR^{2B}R^{2C}, -N(O)_{m2}, -NR^{2B}R^{2C}, -C(O)R^{2D}, -C(O)OR^{2D}, -C(O)NR^{2B}R^{2C}, -OR^{2A}, -NR^{2B}SO₂R^{2A}, -NR^{2B}C(O)R^{2D}, -NR^{2B}C(O)OR^{2D}, -NR^{2B}OR^{2D}, -OCX^{2.1}₃, -OCHX^{2.1}₂, -OCH₂X^{2.1}, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R^{3.2} and R^{3.3} are independently halogen;

R⁴ is hydrogen, halogen, $-CX^{4.1}_3$, $-CHX^{4.1}_2$, $-CH_2X^{4.1}$, $-CN$, $-N_3$, $-SO_{n4}R^{4A}$, $-SO_{v4}NR^{4B}R^{4C}$, $-NHN R^{4B}R^{4C}$, $-ONR^{4B}R^{4C}$, $-NHC(O)NHN R^{4B}R^{4C}$, $-NHC(O)NR^{4B}R^{4C}$, $-N(O)_{m4}$, $-NR^{4B}R^{4C}$, $-C(O)R^{4D}$, $-C(O)OR^{4D}$, $-C(O)NR^{4B}R^{4C}$, $-OR^{4A}$, $-NR^{4B}SO_2R^{4A}$, $-NR^{4B}C(O)R^{4D}$, $-NR^{4B}C(O)OR^{4D}$, $-NR^{4B}OR^{4D}$, $-OCX^{4.1}_3$, $-OCHX^{4.1}_2$, $-OCH_2X^{4.1}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, or when X² is CR⁹, then R⁴ and R⁹ may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R⁷ is hydrogen, halogen, $-CX^{7.1}_3$, $-CHX^{7.1}_2$, $-CH_2X^{7.1}$, $-CN$, $-N_3$, $-SO_{n7}R^{7A}$, $-SO_{v7}NR^{7B}R^{7C}$, $-NHN R^{7B}R^{7C}$, $-ONR^{7B}R^{7C}$, $-NHC(O)NHN R^{7B}R^{7C}$, $-NHC(O)NR^{7B}R^{7C}$, $-N(O)_{m7}$, $-NR^{7B}R^{7C}$, $-C(O)R^{7D}$, $-C(O)OR^{7D}$, $-C(O)NR^{7B}R^{7C}$, $-OR^{7A}$, $-NR^{7B}SO_2R^{7A}$, $-NR^{7B}C(O)R^{7D}$, $-NR^{7B}C(O)OR^{7D}$, $-NR^{7B}OR^{7D}$, $-OCX^{7.1}_3$, $-OCHX^{7.1}_2$, $-OCH_2X^{7.1}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl;

R⁹ is hydrogen, halogen, $-CX^{9.1}_3$, $-CHX^{9.1}_2$, $-CH_2X^{9.1}$, $-CN$, $-N_3$, $-SO_{n9}R^{9A}$, $-SO_{v9}NR^{9B}R^{9C}$, $-NHN R^{9B}R^{9C}$, $-ONR^{9B}R^{9C}$, $-NHC(O)NHN R^{9B}R^{9C}$, $-NHC(O)NR^{9B}R^{9C}$, $-N(O)_{m9}$, $-NR^{9B}R^{9C}$, $-C(O)R^{9D}$, $-C(O)OR^{9D}$, $-C(O)NR^{9B}R^{9C}$, $-OR^{9A}$, $-NR^{9B}SO_2R^{9A}$, $-NR^{9B}C(O)R^{9D}$, $-NR^{9B}C(O)OR^{9D}$, $-NR^{9B}OR^{9D}$, $-OCX^{9.1}_3$, $-OCHX^{9.1}_2$, $-OCH_2X^{9.1}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, or when X² is CR⁹, then R⁴ and R⁹ may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; or when X² is CR⁹ and X³ is CR¹⁰, then R⁹ and R¹⁰ may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R¹⁰ is hydrogen, halogen, $-CX^{10.1}_3$, $-CHX^{10.1}_2$, $-CH_2X^{10.1}$, or $-CN$, $-N_3$, $-SO_{n10}R^{10A}$, $-SO_{v10}NR^{10B}R^{10C}$, $-NHN R^{10B}R^{10C}$, $-ONR^{10B}R^{10C}$, $-NHC(O)NHN R^{10B}R^{10C}$, $-NHC(O)NR^{10B}R^{10C}$, $-N(O)_{m10}$, $-NR^{10B}R^{10C}$, $-C(O)R^{10D}$, $-C(O)OR^{10D}$, $-C(O)NR^{10B}R^{10C}$, $-OR^{10A}$, $-NR^{10B}SO_2R^{10A}$, $-NR^{10B}C(O)R^{10D}$, $-NR^{10B}C(O)OR^{10D}$, $-NR^{10B}OR^{10D}$, $-OCX^{10.1}_3$, $-OCHX^{10.1}_2$, $-OCH_2X^{10.1}$, substituted or unsubstituted alkyl, substituted or unsubstituted

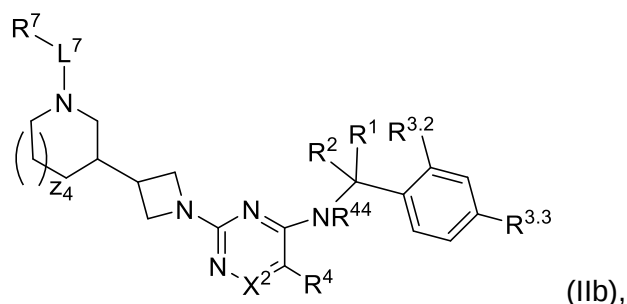
heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; or when X^2 is CR^9 and X^3 is CR^{10} , then R^9 and R^{10} may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

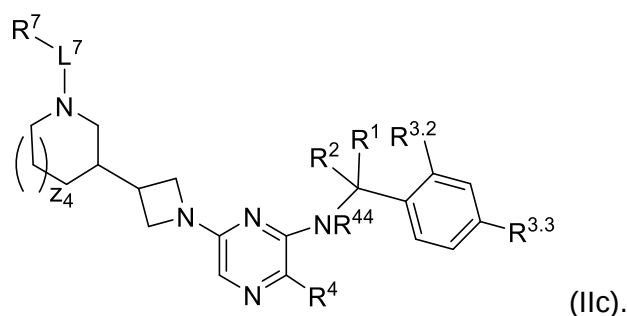
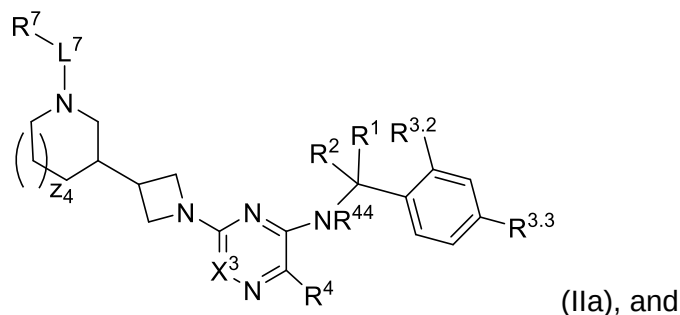
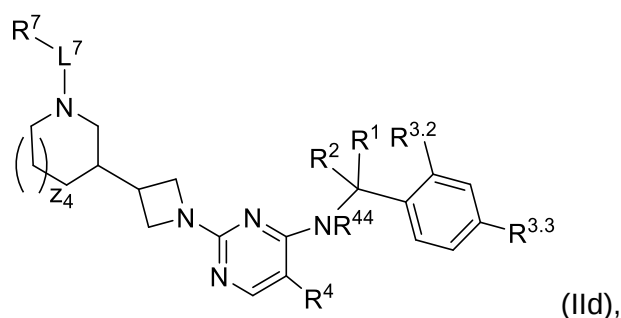
R^{44} is hydrogen, $-CX^{44.1}_3$, $-CHX^{44.1}_2$, $-CH_2X^{44.1}$, $-SO_{n44}R^{44A}$, $-SO_{v44}NR^{44B}R^{44C}$, $-C(O)R^{44D}$, $-C(O)OR^{44D}$, $-C(O)NR^{44B}R^{44C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted C_3 - C_8 cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl;

R^{1A} , R^{1B} , R^{1C} , R^{1D} , R^{2A} , R^{2B} , R^{2C} , R^{2D} , R^{4A} , R^{4B} , R^{4C} , R^{4D} , R^{7A} , R^{7B} , R^{7C} , R^{7D} , $R^{7.2B}$, R^{9A} , R^{9B} , R^{9C} , R^{9D} , R^{10A} , R^{10B} , R^{10C} , R^{10D} , R^{44A} , R^{44B} , R^{44C} , and R^{44D} are independently hydrogen, halogen, $-CF_3$, $-CCl_3$, $-CBr_3$, $-Cl_3$, $-COOH$, $-CONH_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{1B} , R^{1C} , R^{2B} , R^{2C} , R^{4B} , R^{4C} , R^{7B} , R^{7C} , R^{9B} , R^{9C} , R^{10B} , R^{10C} , R^{44B} , and R^{44C} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; and $X^{1.1}$, $X^{2.1}$, $X^{4.1}$, $X^{7.1}$, $X^{9.1}$, $X^{10.1}$, and $X^{44.1}$ are independently $-Cl$, $-Br$, $-I$ or $-F$; wherein at least one of X^2 and X^3 is N.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein z_4 is 1.

3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has one of structural Formula (IIb), (IIc), (IIa), or (IIc):





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

X^2 is CR^9 ;

X^3 is CR^{10} ;

R^9 is hydrogen, $-CX^{9.1}_3$, $-CHX^{9.1}_2$, $-CH_2X^{9.1}$, $-CN$, or substituted or unsubstituted C_1 - C_4 alkyl, optionally wherein R^9 is hydrogen, $-CF_3$, or unsubstituted methyl; and

R^{10} is hydrogen, $-CX^{10.1}_3$, $-CHX^{10.1}_2$, $-CH_2X^{10.1}$, $-CN$, or substituted or unsubstituted alkyl, optionally wherein R^{10} is hydrogen or $-CN$.

5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen, halogen, $-CX^{4.1}_3$, $-CHX^{4.1}_2$, $-CH_2X^{4.1}$, $-CN$, $-NR^{4B}R^{4C}$, $-C(O)R^{4D}$, $-C(O)OR^{4D}$, $-C(O)NR^{4B}R^{4C}$, $-OR^{4A}$, $-NR^{4B}C(O)R^{4D}$, $-NR^{4B}C(O)OR^{4D}$, $-OCX^{4.1}_3$, $-OCHX^{4.1}_2$, $-OCH_2X^{4.1}$, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl, optionally wherein R^4 is $-Cl$, $-Br$, $-F$, -

CN, -COOH, -C(O)OCH₂CH₃, -C(CH₃)₂OH,
-C(O)NH₂, -CF₃, or -CH₃.

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

X² is CR⁹; and

R⁴ and R⁹ are joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, optionally wherein R⁴ and R⁹ are joined to form an unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted phenyl, or unsubstituted heteroaryl, further optionally wherein R⁴ and R⁹ are joined to form an unsubstituted cycloalkyl, unsubstituted thienyl, or unsubstituted phenyl.

7. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁴⁴ is hydrogen.

8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ and R² are independently hydrogen, substituted or unsubstituted alkyl or substituted or unsubstituted heteroalkyl, optionally wherein one of R¹ and R² is hydrogen and the other is -CH₃.

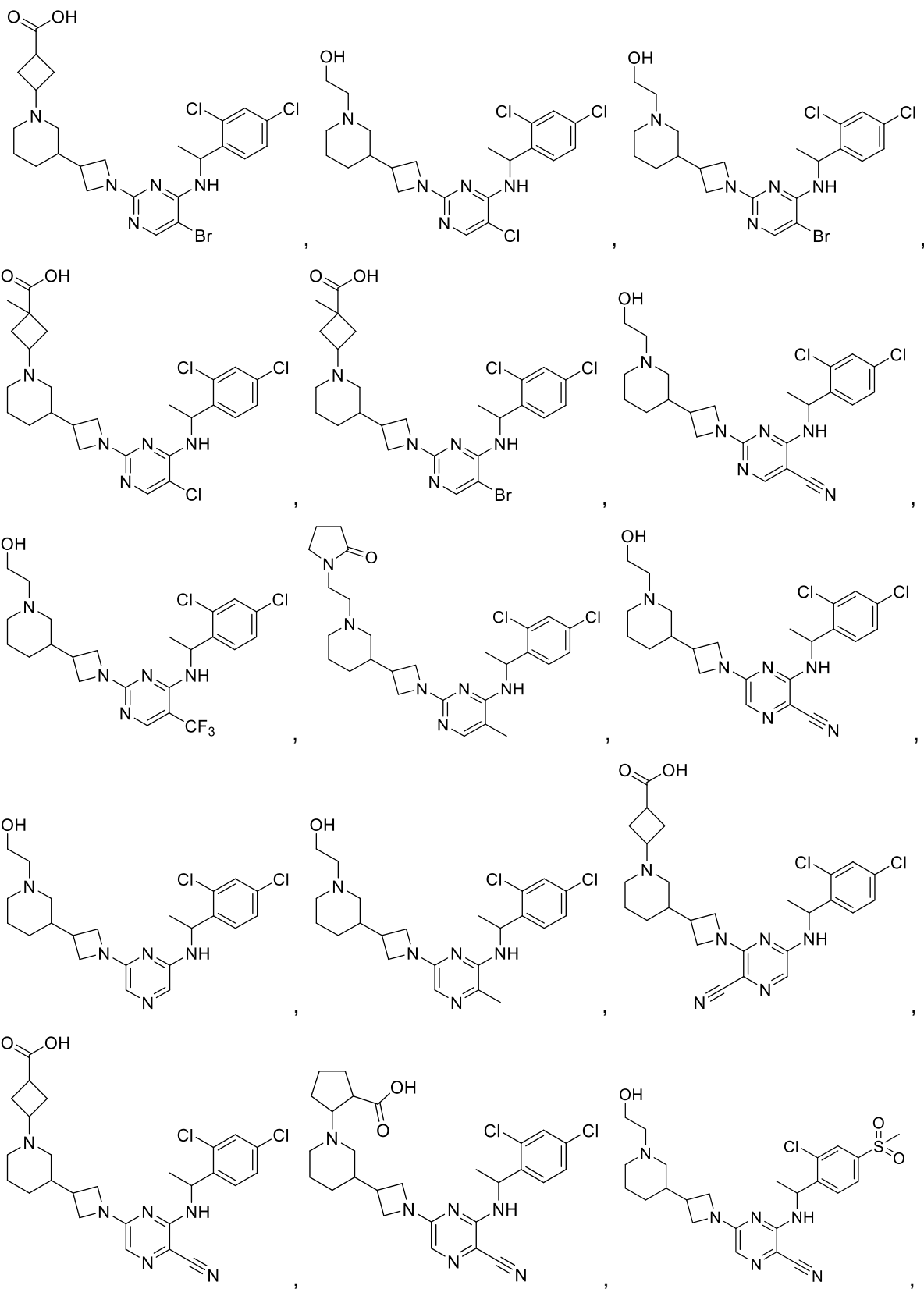
9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^{3,2} and R^{3,3} are independently chlorine.

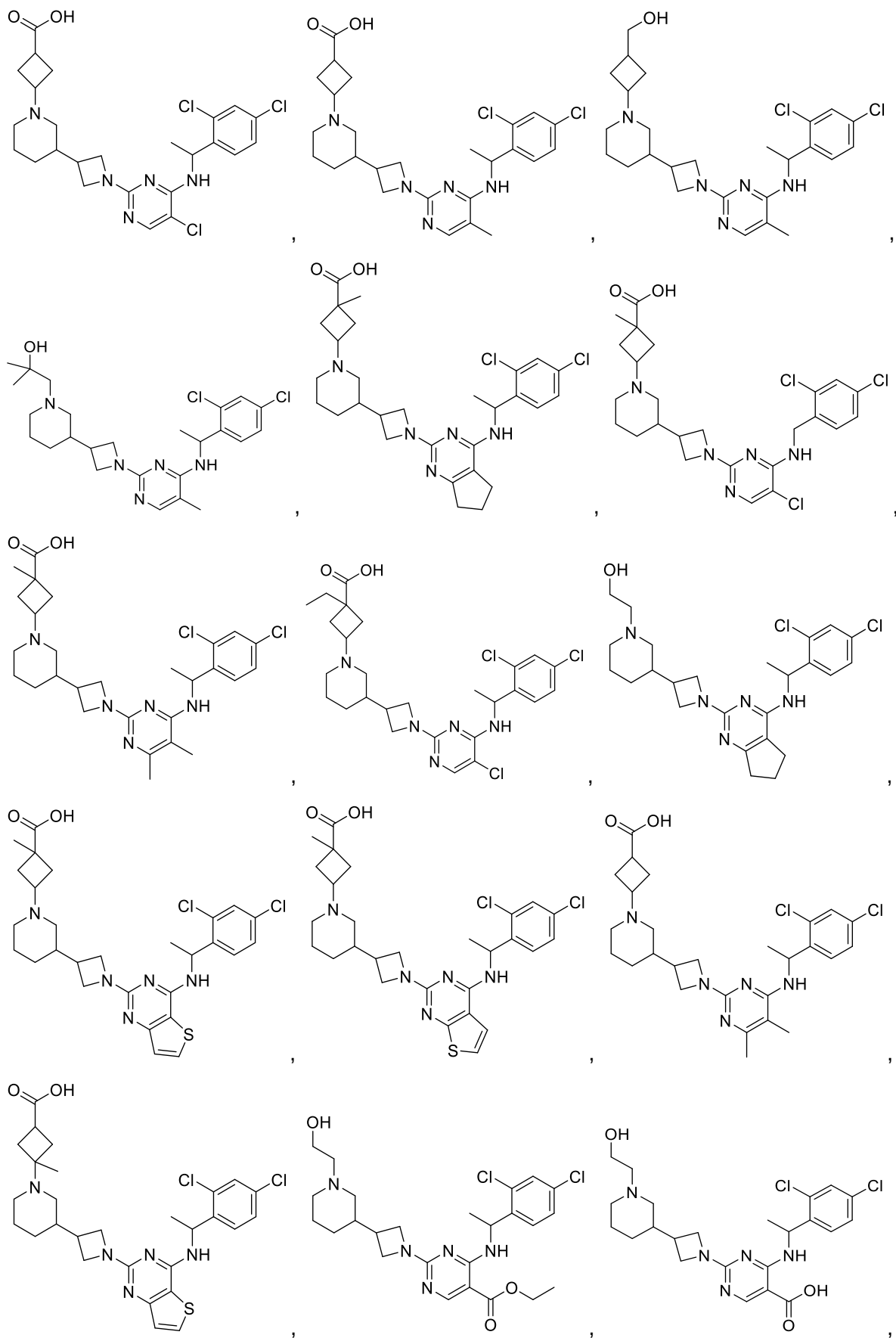
10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein L⁷ is a bond, substituted or unsubstituted alkylene, or substituted or unsubstituted cycloalkylene, optionally wherein L⁷ is a bond, an unsubstituted cycloalkylene, a substituted or unsubstituted cyclobutylene or a substituted or unsubstituted alkylene.

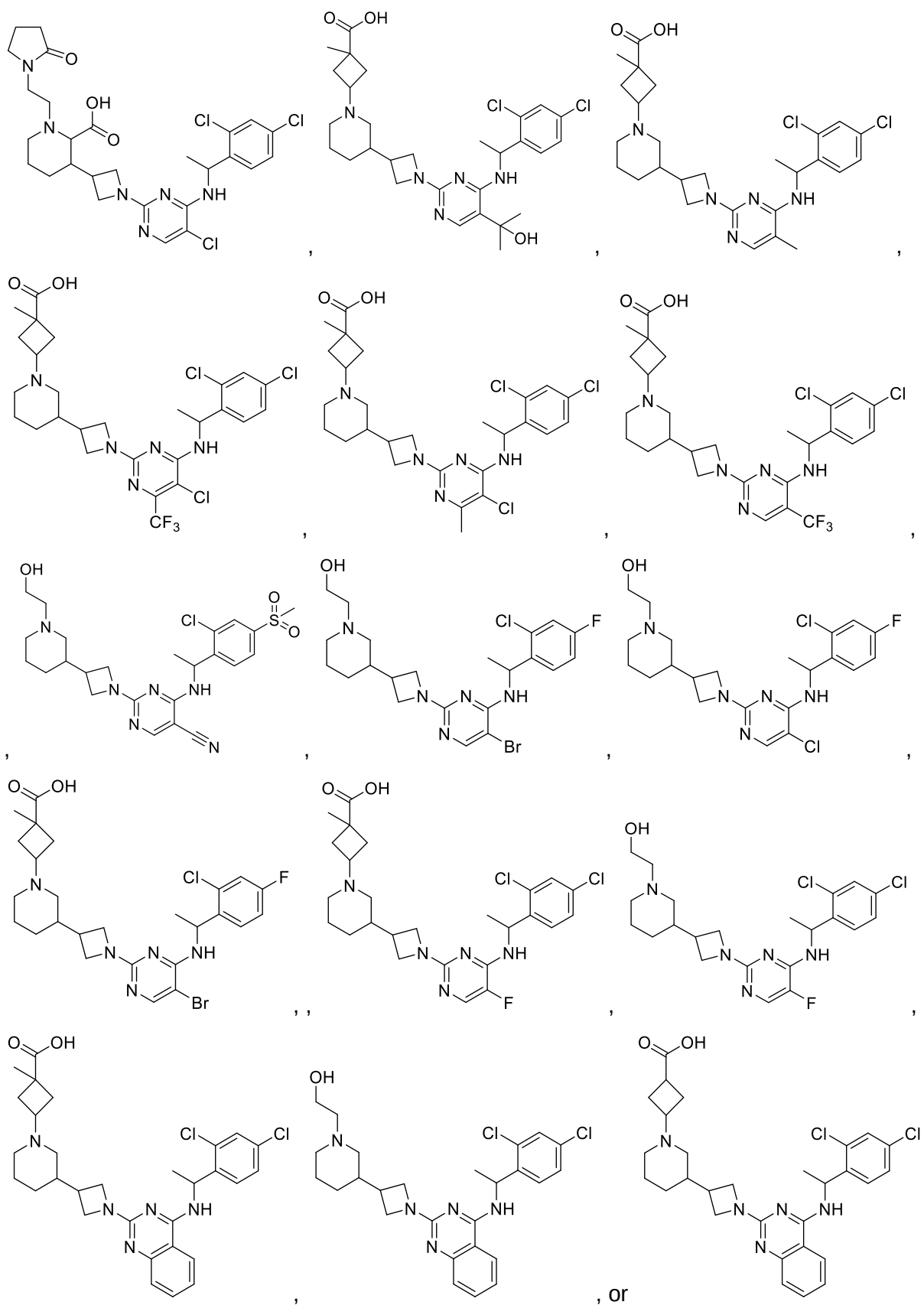
11. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁷ is hydrogen, halogen, -SO_{n7}R^{7A}, -SO_{v7}NR^{7B}R^{7C}, -NHC(O)NR^{7B}R^{7C}, -NR^{7B}R^{7C}, -C(O)R^{7D}, -C(O)OR^{7D}, -C(O)NR^{7B}R^{7C}, -OR^{7A}, -NR^{7B}SO₂R^{7A}, -NR^{7B}C(O)R^{7D}, -

*CO, *C1CCCC1C(=O)O, *CCN1CCCC1=O, *C12CCC(C1)C(=O)O2, *C12CCC(C1)(C)C(=O)O2,
*C12CCC(C1)C(=O)O2, or *C12CCC(C1)C(=O)O2CC.

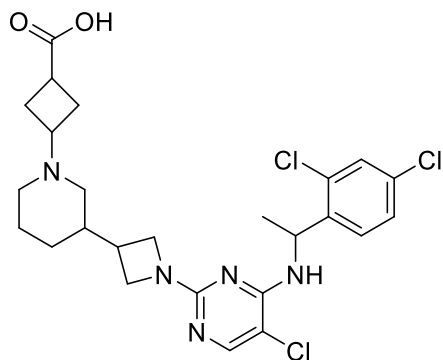
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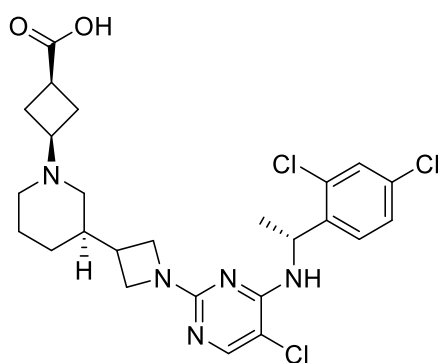




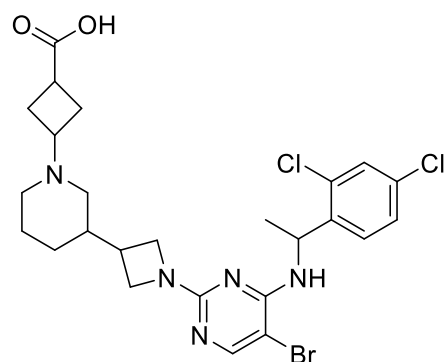
14. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compounds has the structure:

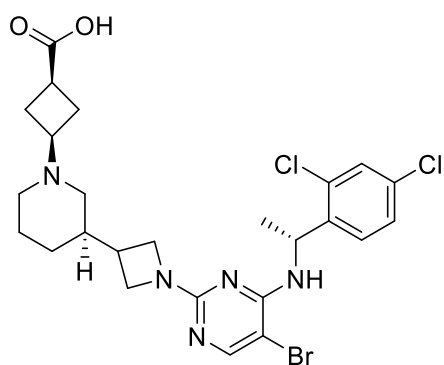


or



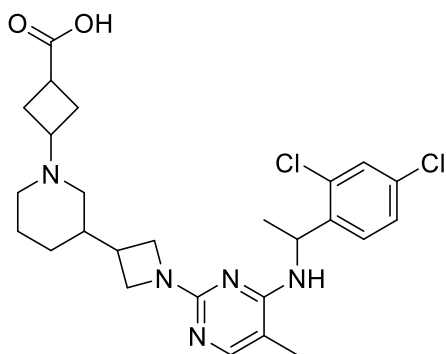
15. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has the structure:



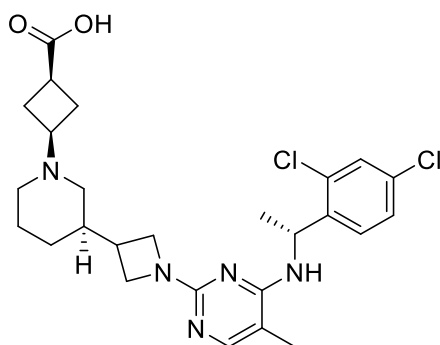


or

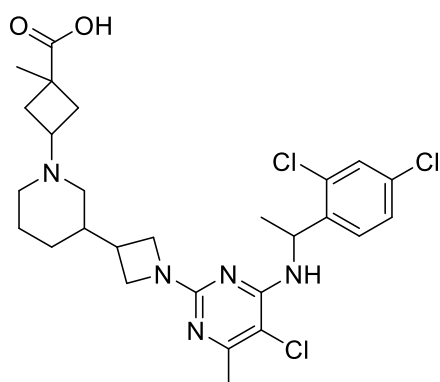
16. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has the structure:



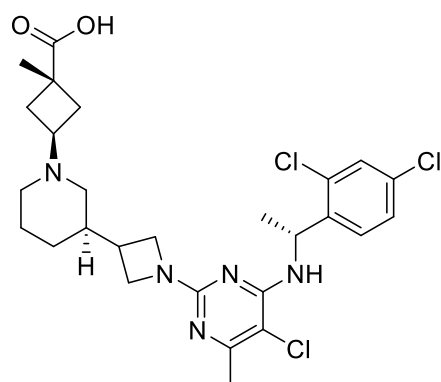
or



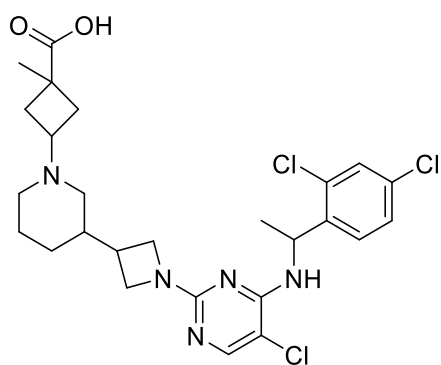
17. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has the structure:



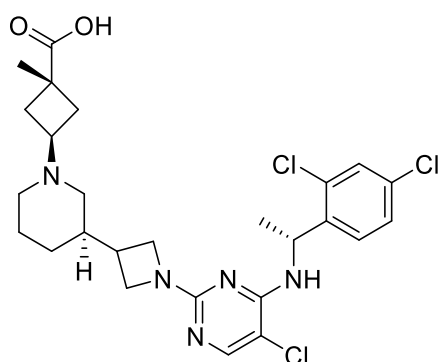
or



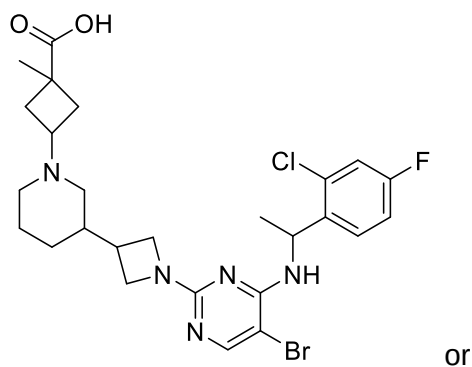
18. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has the structure:



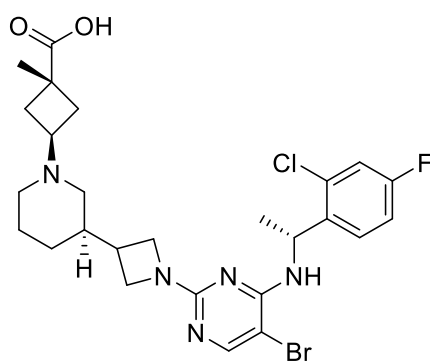
or



19. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has the structure:



or



20. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of any one of claim 1 to 19, or a pharmaceutically acceptable salt thereof.

21. The compound of any one of claims 1 to 19 for use as a medicament for treating or preventing a disease or disorder mediated by CCR4, wherein the disease or

disorder is an immune disease or disorder, inflammatory disease or disorder, cardiovascular disease or disorder, metabolic disease or disorder, or cancer.

22. The pharmaceutical composition of claim 20 for use as a medicament for treating or preventing a disease or disorder mediated by CCR4, wherein the disease or disorder is an immune disease or disorder, inflammatory disease or disorder, cardiovascular disease or disorder, metabolic disease or disorder, or cancer.

23. The compound of any one of claims 1 to 19 for use as a medicament for inhibiting C-C chemokine receptor type 4 (CCR4).

24. The compound for use of claim 21, optionally adapted for co-administration with an anti-inflammatory agent, a cardiovascular agent, a metabolic disorder agent, a chemotherapeutic agent or anticancer agent to the subject,

wherein the anti-inflammatory agent is thalidomide or a derivative thereof, a retinoid, dithranol, calcipotriol, a non-steroidal anti-inflammatory agent (NSAID), a cyclo-oxygenase inhibiting nitric oxide donor (CINOD), a glucocorticosteroid, methotrexate, leflunomide, hydroxychloroquine, d-penicillamine, auranofin, an analgesic, a diacerein, or hyaluronic acid derivative;

wherein the cardiovascular agent is a calcium channel blocker, a beta-adrenoceptor blocker, an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin-2 receptor antagonist, a lipid lowering agent, a modulator of blood cell morphology, a thrombolytic, or an anticoagulant; and

wherein the chemotherapeutic agent or anticancer agent is an antiproliferative/antineoplastic drug, an antimetabolite, an antitumour antibiotic, an antimitotic agent, a topoisomerase inhibitor, a cytostatic agent, an oestrogen receptor down regulator, an antiandrogen, a LHRH antagonist or LHRH agonist, a progestogen, an aromatase inhibitor, an inhibitor of 5 α -reductase, an agent which inhibits cancer cell invasion, an inhibitor of growth factor function, a farnesyl transferase inhibitor, a tyrosine kinase inhibitor, a serine/threonine kinase inhibitor, an inhibitor of the epidermal growth factor family, an inhibitor of the platelet-derived growth factor family, an inhibitor of the hepatocyte growth factor family; an antiangiogenic agent, a vascular damaging agent, an agent used in antisense therapy, an anti-ras antisense, an agent used in a gene therapy, an immunotherapeutic agent, or an antibody.

25. The compound for use of claim 24, wherein the chemotherapeutic agent or anticancer agent is an inhibitor of the PD-L1/PD-1 pathway, an inhibitor of CTLA-4 or an agonistic antibody of CD137 (4-1BB).

26. The compound for use of claim 24 optionally adapted for co-administration with an immune modulator agent, wherein the immune modulator agent is TSR-022, MGB453, BMS-986016, IMP321, MGA271, MGD-009, RG-6058, AMG 557, SEA-CD40, dacetuzumab, CP-870,893, Chi Lob 7/4, lucatumumab, galiximab, INCAGN1876, TRX518, MEDI-570, MEDI-6469, INCAGN1949, huMab OX40L, monalizumab, galunisertib, luspatercept, YH-14618, dalantercept, BG-00011, trabedersen, isth-0036, ace-083, NKTR-214, recombinant IL2, aldesleukin, EGEN-001, NHS-IL12, recombinant IL-7, NIZ-985, ALT-803, recombinant IL-21, anti-CD20.IL21, tralokinumab, dupilumab, cabiralizumab, INCB50465, idealisib, TGR-1202, AMG319, IPI-549, azacytidine, decitabine, guadecitabine, vorinostat, panobinostat, belinostat, entinostat, mocetinostat, givinostat, chidamide, quisinostat, abexinostat, chr-3996, ar-42, INCN54329, INCB57643, birabresib, apabetalone, alvocidib, PLX-51107, FT-1101, RG-6146, AZD-8186, CPI-0610, JQ1, INCB59872, IMG-7289, RG-6016, CC-90011, GSK-2879552, ORY-2001, 4SC-202, ORY-3001, recombinant TNFa, MEDI-1873, FPA-154, LKZ-145, recombinant IL1, recombinant interferon alpha-n1, recombinant interferon alpha-2b, recombinant interferon alpha-n3, recombinant IFN beta-1a, actimmune, cyclic di-nucleotides, poly I:C, IMO-2055, TMX-101, imiquimod, CpG, MGN1703, glucopyranosyl lipid A, CBLB502, BCG, HILTONOL, AMPLIGEN, MOTOLIMOD, DUK-CPG-001, AS15, recombinant IL-10, CCX140, CCX872, BMS-813160, CENICRIVIROC, CNTX-6970, PF-4136309, plozalizumab, INCB-9471, PF-04634817, maraviroc, PRO-140, BMS-813160, NIFEVIROC, OHR-118, ulocuplumab, plerixafor, x4p-001, usl-311, ly-2510924, APH-0812, BL-8040, BURIXAFOR, BALIXAFORTIDE, PTX-9908, GMI-1359, F-50067, IPH-4301, CA-170, ISTRADEFYLLINE, TOZADENANT, PBF-509, PBF-999, CPI-444, OREG-103, anti-CD39 antibodies, oleclumab, PBF-1662, anti-CD73 antibodies, pembrolizumab, nivolumab, INCSHR1210, CT-011, AMP224, atezolizumab, avelumab, tremelimumab, urelumab, utomilumab, BMS-663513, PF-05082566, BGB-324, BPI-9016M, S-49076, ibrutinib, Cb-1158, MDX-1140, AMP-110, PT2385, CDX-301, FLX925, quizartinib, gilteritinib, PKC412, midostaurin, crenolanib, lirlumab, IPH-2101, anti-CD47, TTI-621, NI-1701, SRF-231, Effi-DEM, RCT-1938, epacadostat, F287, BMS983205, GDC-0919, or indoximod, or any combination thereof.

27. The compound for use of claim 21 wherein the cancer is colon cancer or pancreatic cancer.

28. The compound for use of claim 21, wherein the disease or disorder is allergy-related.

29. The compound for use of claim 21, wherein the disease or disorder is inflammation, wherein the inflammation is asthma, urticaria, rhinitis, or dermatitis.

30. The compound for use of claim 29, wherein the inflammation is allergic asthma, autoimmune urticaria, allergic rhinitis or contact dermatitis.