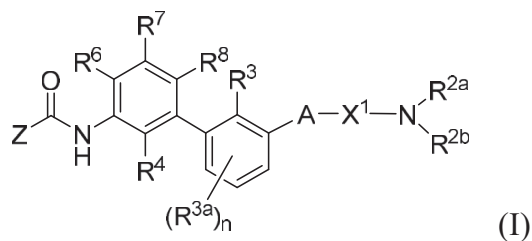


CLAIMS:

1. A compound of Formula (I):



or a pharmaceutically acceptable salt, or a stereoisomer thereof, wherein:

A is a 5- to 6-membered heteroaryl group which is unsubstituted or substituted with from one to three members independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy and CN;

X¹ is C₁₋₃ alkylene, which is unsubstituted or substituted with one or two members independently selected from the group consisting of C₁₋₂ alkyl and CO₂H;

R^{2a} and R^{2b} are each independently selected from the group consisting of H, C₁₋₈ alkyl, C₁₋₈ haloalkyl, -Y, -X²-CO₂R^a, -X²-OR^a, -X²-NR^aR^b, -X²-C(O)NR^aR^b, -X²-SO₂R^a, -X²-SO₂NR^aR^b, -X²-SO₃R^a and -X²-Y, wherein each X² is C₁₋₆ alkylene, any C₁₋₈ alkyl or C₁₋₆ alkylene is unsubstituted or substituted with one or two members independently selected from the group consisting of OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂-C₁₋₈ alkyl and CO₂H, and each Y is selected from the group consisting of C₃₋₆ cycloalkyl, C₄₋₈ heterocyclyl and 5- to 6-membered heteroaryl, each of which is unsubstituted or substituted with one to four substituents independently selected from the group consisting of oxo, OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₁₋₄ hydroxyalkoxy, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl, SO₃H and CO₂H;

or R^{2a} and R^{2b} are combined to form a 4- to 9-membered ring or spirocyclic ring, having from zero to two additional heteroatom ring vertices selected from O, N or S;

wherein the ring formed by combining R^{2a} and R^{2b}, is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of oxo, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₁₋₈ hydroxyalkyl, -X³-CO₂R^a, -X³-OR^a, -X³-NR^aR^b,

$-X^3-C(O)NR^aR^b$, $-X^3-SO_2R^a$, $-X^3-SO_2NR^aR^b$, and $-X^3-SO_3R^a$; wherein X^3 is a bond or C_{1-6} alkylene;

R^3 and R^4 are each independently selected from the group consisting of F, Cl, CN, CH_3 , OCH_3 , CH_2CH_3 and CF_3 ;

the subscript n is 0, 1, 2 or 3;

each R^{3a} is independently selected from the group consisting of H, F, Cl, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, C_{2-3} alkenyl and CN;

R^6 , R^7 and R^8 are each independently selected from the group consisting of H, F, Cl, CN, CH_3 , OCH_3 , CH_2CH_3 and CF_3 ;

Z is

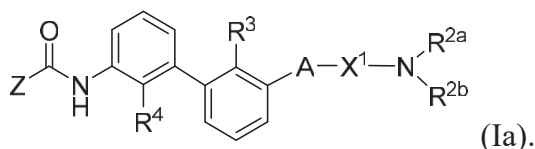
a monocyclic non-aromatic heterocyclic ring, optionally substituted with one or two oxo groups and optionally substituted with up to four R^a and/or R^b ;

each R^a is independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkylene- CO_2H , and C_{1-6} alkylene- SO_3H ;

each R^b is independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkylene- CO_2H , and C_{1-6} alkylene- SO_3H , each of which is unsubstituted or substituted with one or two members independently selected from OH, SO_2NH_2 , $C(O)NH_2$, $C(O)NHOH$, PO_3H_2 , CO_2C_{1-8} alkyl and CO_2H ;

and R^a and R^b , when attached to the same nitrogen atom, are optionally combined to form a 4- to 8-membered ring or spirocyclic ring, which is unsubstituted or substituted with halogen, OH, SO_2NH_2 , $C(O)NH_2$, $C(O)NHOH$, PO_3H_2 , CO_2C_{1-8} alkyl or CO_2H .

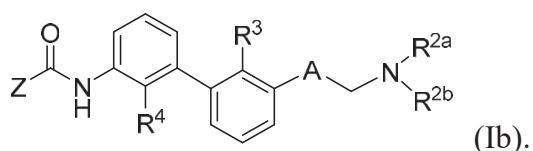
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having formula (Ia):



3. The compound of any one of claims 1 to 2, or a pharmaceutically acceptable salt thereof, wherein A is a 5- or 6-membered heteroaryl group which is unsubstituted or substituted with from one to three members independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, and CN.

4. The compound of any one of claims 1 to 2, or a pharmaceutically acceptable salt thereof, wherein A is a 6-membered heteroaryl group which is unsubstituted or substituted with from one to three members independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, and CN.

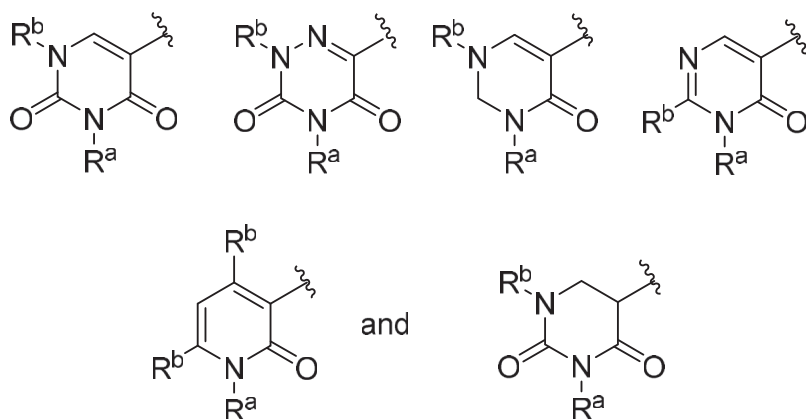
5. The compound of any one of claims 1 to 4 a pharmaceutically acceptable salt thereof, having formula (Ib):



6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein A is unsubstituted or substituted with one or two members independently selected from the group consisting of OCH₃ and F.

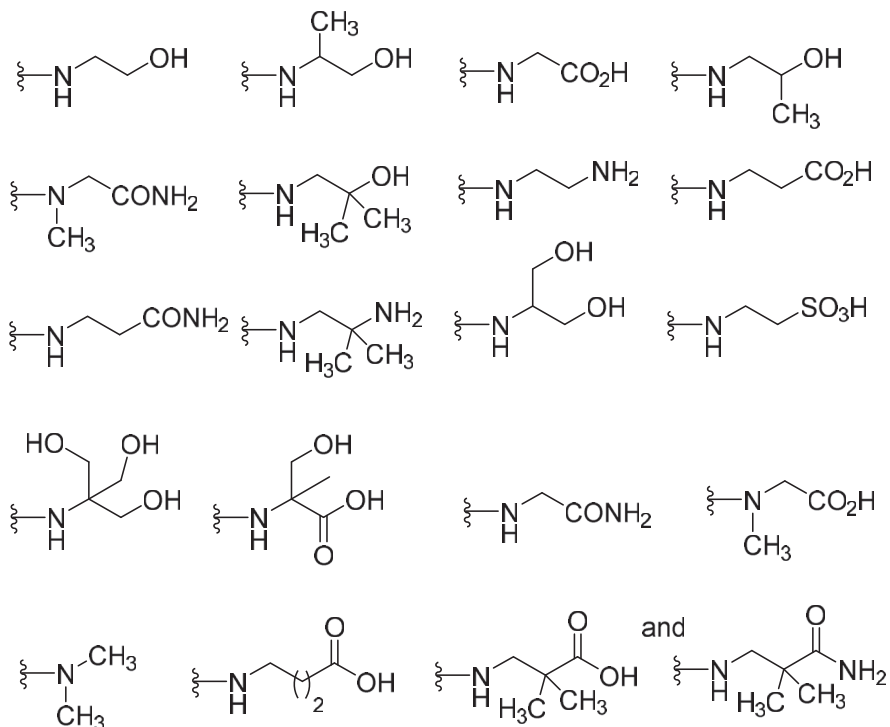
7. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein A is a 6-membered heteroaryl selected from the group consisting of pyridine, pyrimidine, pyrazine and 1,2,4-triazine, each of which is unsubstituted or substituted with one or two members independently selected from the group consisting of OCH₃ and F.

8. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein Z is a non-aromatic heterocyclic ring having a formula selected from the group consisting of:

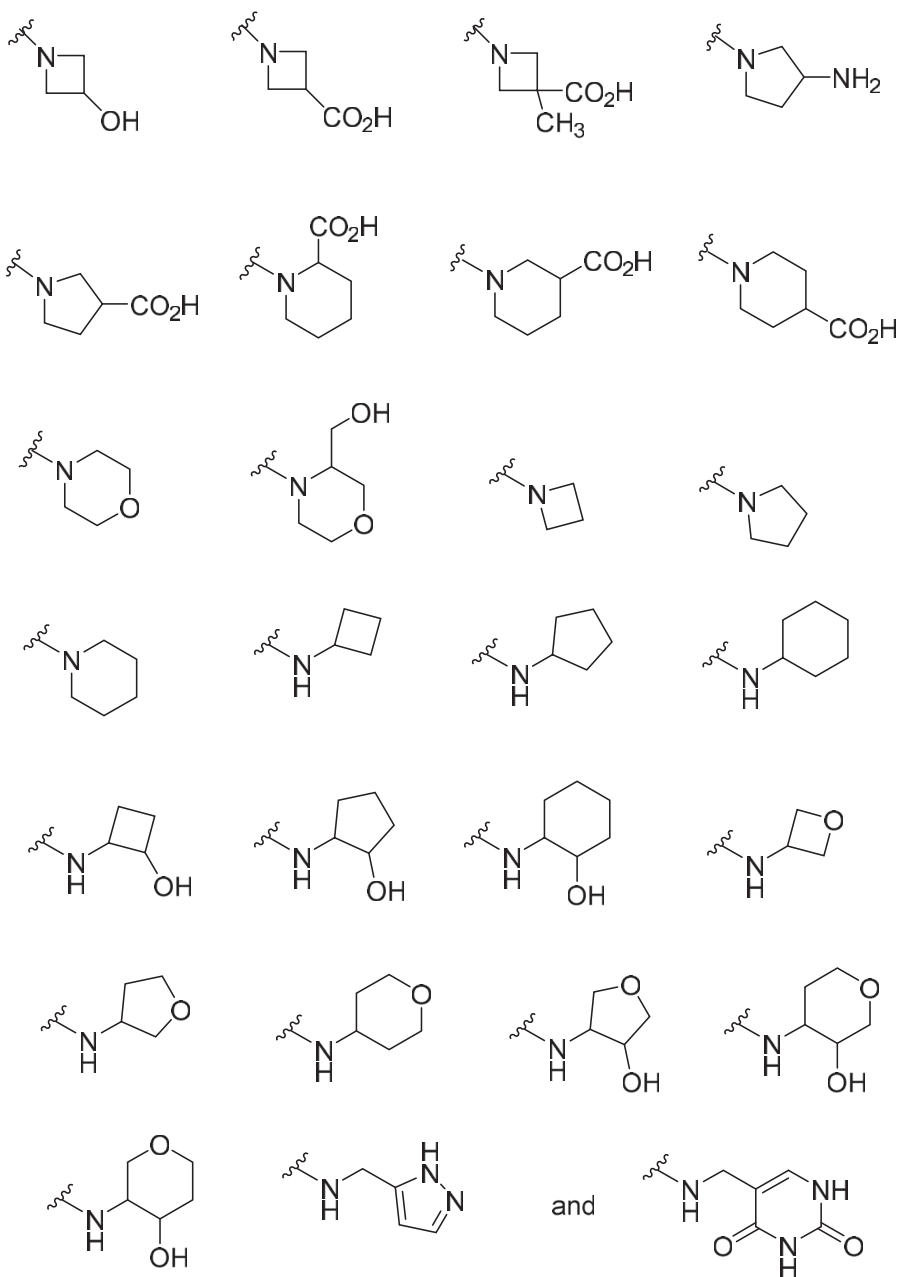


9. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein Z is a non-aromatic heterocyclic ring selected from the group consisting of piperidinyl, morpholinyl, tetrahydropyranyl, and tetrahydrofuranyl, each of which is optionally substituted with up to four R^a and/or R^b .

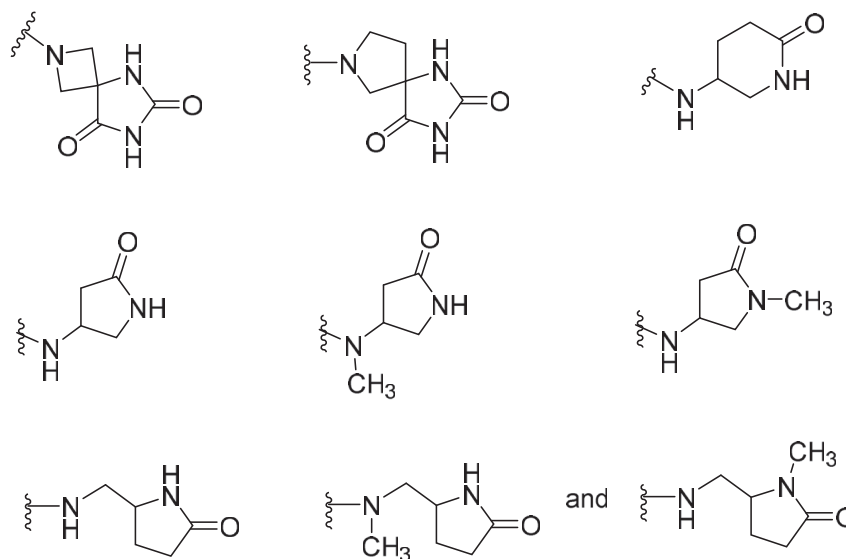
10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein $-N(R^{2a})(R^{2b})$ is selected from the group consisting of:



11. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein $-N(R^{2a})(R^{2b})$ is selected from the group consisting of:



12. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein $-N(R^{2a})(R^{2b})$ is selected from the group consisting of:



13. The compound of any one of claims **1** to **12**, or a pharmaceutically acceptable salt thereof, wherein the compound is an optically pure or enriched stereoisomer.

14. The compound of any one of claims **1** to **12**, or a pharmaceutically acceptable salt thereof, wherein Y is selected from the group consisting of C₃₋₆ cycloalkyl and C₄₋₈ heterocyclyl, each of which is unsubstituted or substituted with one to four substituents independently selected from the group consisting of oxo, OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₁₋₄ hydroxyalkoxy, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl, SO₃H and CO₂H.

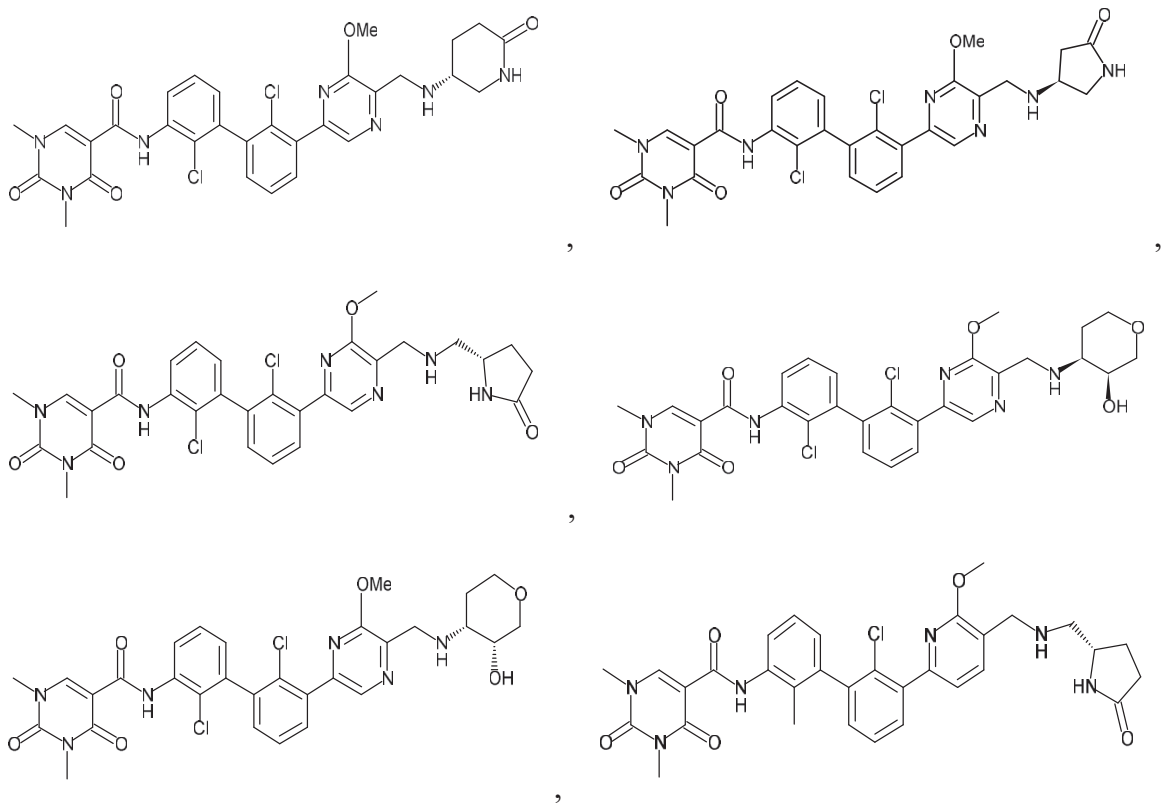
15. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein Z is a 5- or 6-membered non-aromatic heterocyclic ring, optionally substituted with one or two oxo groups and optionally substituted with R^a and/or R^b.

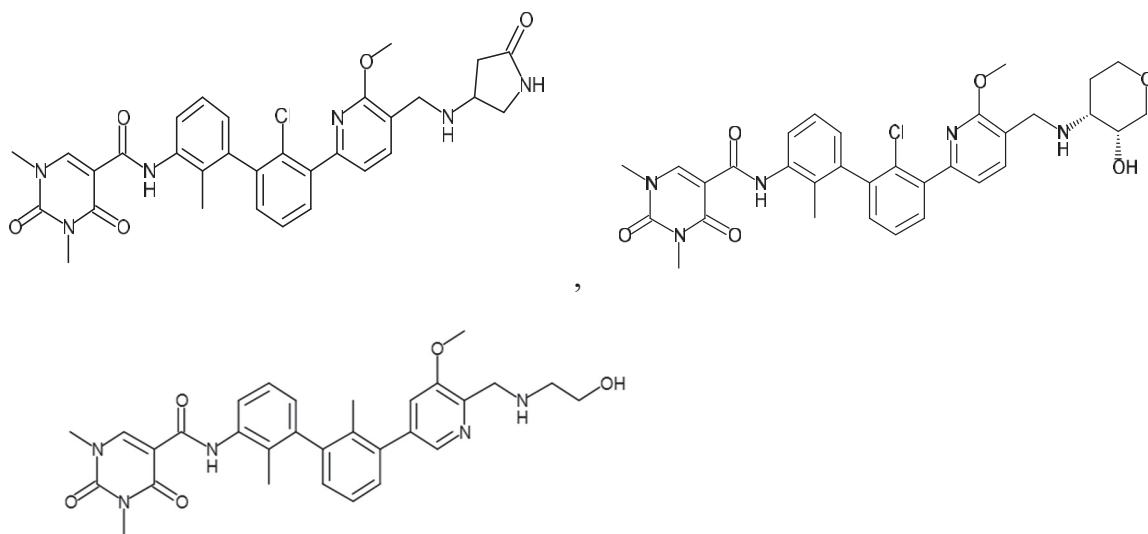
16. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein Z is a 5- or 6-membered monocyclic non-aromatic heterocyclic ring, optionally substituted with one or two oxo groups and optionally substituted with R^a and/or R^b; and each of R⁶, R⁷ and R⁸ is H.

17. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein Z is a 5- or 6-membered non-aromatic heterocyclic ring selected from the

group consisting of piperidinyl, morpholinyl, tetrahydropyranyl, and tetrahydrofuranyl, optionally substituted with one or two oxo groups and optionally substituted with R^a and/or R^b.

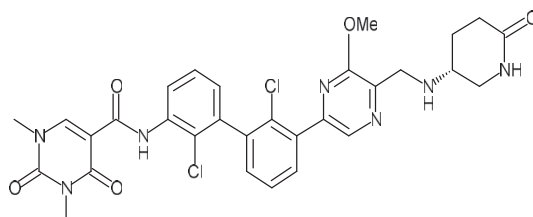
18. The compound of claim 1, wherein said compound is selected from the group consisting of





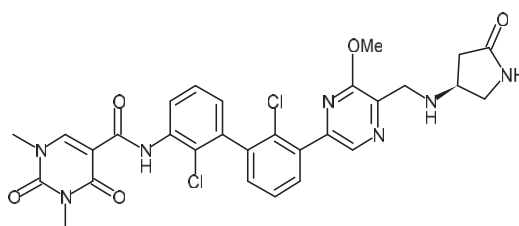
or a pharmaceutically acceptable salt thereof.

19. The compound of claim **1**, having the formula



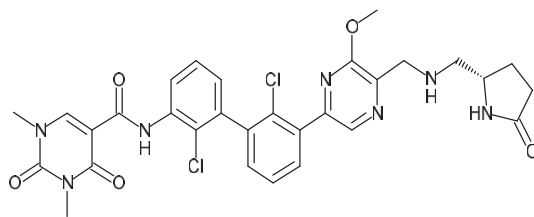
or a pharmaceutically acceptable salt thereof.

20. The compound of claim **1**, having the formula



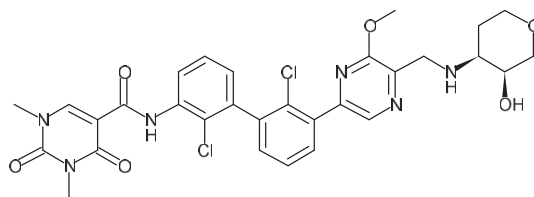
or a pharmaceutically acceptable salt thereof.

21. The compound of claim **1**, having the formula



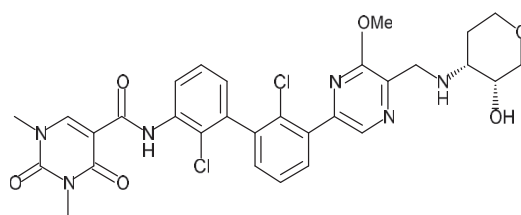
or a pharmaceutically acceptable salt thereof.

22. The compound of claim 1, having the formula



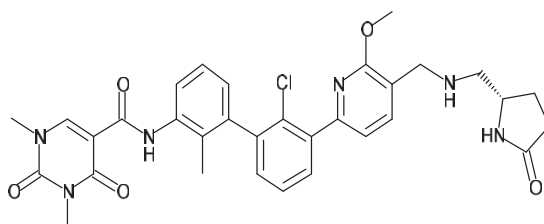
or a pharmaceutically acceptable salt thereof.

23. The compound of claim 1, having the formula



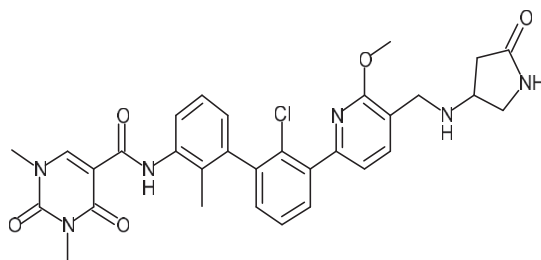
or a pharmaceutically acceptable salt thereof.

24. The compound of claim 1, having the formula



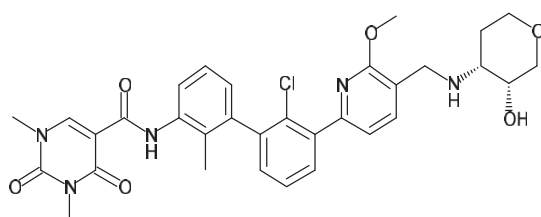
or a pharmaceutically acceptable salt thereof.

25. The compound of claim 1, having the formula



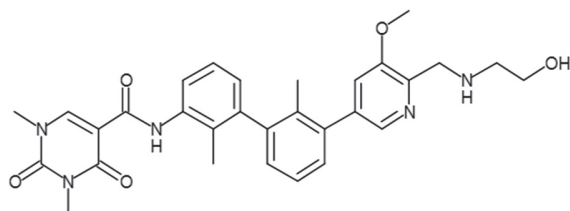
or a pharmaceutically acceptable salt thereof.

26. The compound of claim **1**, having the formula



or a pharmaceutically acceptable salt thereof.

27. The compound of claim **1**, having the formula



or a pharmaceutically acceptable salt thereof.

28. A pharmaceutical composition comprising a compound of any one of claims **1** to **27**, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

29. The pharmaceutical composition of claim **28**, further comprising one or more additional therapeutic agents.

30. The pharmaceutical composition of claim **29**, wherein the one or more additional therapeutic agent is selected from the group consisting of an antimicrobial agent,

an antiviral agent, a cytotoxic agent, a gene expression modulatory agent, a chemotherapeutic agent, an anti-cancer agent, an anti-angiogenic agent, an immunotherapeutic agent, an anti-hormonal agent, an anti-fibrotic agent, radiotherapy, a radiotherapeutic agent, an anti-neoplastic agent, and an anti-proliferation agent.

31. Use of a compound of any one of claims **1** to **27**, or a pharmaceutically acceptable salt thereof or a composition of any one of claims **28** to **30**, in the preparation of a medicament for modulating an immune response mediated by the PD-1 signaling pathway in a subject, wherein the subject suffers from a disease or disorder selected from the group consisting of an infectious disease, a bacterial infectious disease, a viral infectious disease, a fungal infectious disease, a solid tumor, a hematological malignancy, an immune disorder, an inflammatory disease, and cancer.

32. Use of a compound of any one of claims **1** to **27**, or a pharmaceutically acceptable salt thereof or a composition of any one of claims **28** to **30**, in the preparation of a medicament for enhancing, stimulating, modulating and/or increasing the immune response in a subject in need thereof, wherein the subject suffers from a disease or disorder selected from the group consisting of an infectious disease, a bacterial infectious disease, a viral infectious disease, a fungal infectious disease, a solid tumor, a hematological malignancy, an immune disorder, an inflammatory disease, and cancer.

33. Use of a compound of any one of claims **1** to **27**, or a pharmaceutically acceptable salt thereof or a composition of any one of claims **28** to **30**, in the preparation of a medicament for inhibiting growth, proliferation, or metastasis of cancer cells in a subject in need thereof.

34. Use of a compound of any one of claims **1** to **27**, or a pharmaceutically acceptable salt thereof or a composition of any one of claims **28** to **30**, in the preparation of a medicament for treating a subject suffering from or susceptible to a disease or disorder mediated by the PD-1 signaling pathway, wherein the disease or disorder is selected from the group consisting of an infectious disease, a bacterial infectious disease, a viral infectious

disease a fungal infectious disease, a solid tumor, a hematological malignancy, an immune disorder, an inflammatory disease, and cancer.

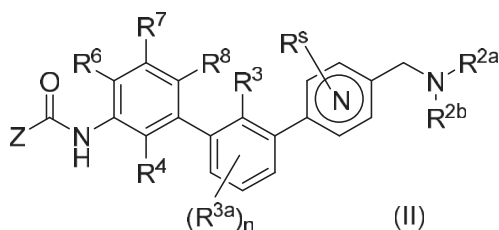
35. The use of claim **34**, wherein the disease or disorder is selected from the group consisting of melanoma, glioblastoma, esophagus tumor, nasopharyngeal carcinoma, uveal melanoma, lymphoma, lymphocytic lymphoma, primary CNS lymphoma, T-cell lymphoma, diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, prostate cancer, castration-resistant prostate cancer, chronic myelocytic leukemia, Kaposi's sarcoma fibrosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, angiosarcoma, lymphangiosarcoma, synovioma, , meningioma, leiomyosarcoma, rhabdomyosarcoma, sarcoma of soft tissue, sarcoma, sepsis, biliary tumor, basal cell carcinoma, thymus neoplasm, cancer of the thyroid gland, cancer of the parathyroid gland, uterine cancer, cancer of the adrenal gland, liver infection, Merkel cell carcinoma, nerve tumor, follicle center lymphoma, colon cancer, Hodgkin's disease, non-Hodgkin's lymphoma, leukemia, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, multiple myeloma, ovary tumor, myelodysplastic syndrome, cutaneous or intraocular malignant melanoma, renal cell carcinoma, small-cell lung cancer, lung cancer, mesothelioma, breast cancer, squamous non-small cell lung cancer (SCLC), non-squamous NSCLC, colorectal cancer, ovarian cancer, gastric cancer, hepatocellular carcinoma, pancreatic carcinoma, pancreatic cancer, Pancreatic ductal adenocarcinoma, squamous cell carcinoma of the head and neck, cancer of the head or neck, gastrointestinal tract, stomach cancer, HIV, Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, herpes viruses, papillomaviruses, influenza, bone cancer, skin cancer, rectal cancer, cancer of the anal region, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the urethra, cancer of the penis, cancer of the bladder, cancer of the kidney, cancer of the ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, epidermoid cancer, abestosis, carcinoma, adenocarcinoma, papillary carcinoma,

cystadenocarcinoma, bronchogenic carcinoma, renal cell carcinoma, transitional cell carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, wilm's tumor, pleomorphic adenoma, liver cell papilloma, renal tubular adenoma, cystadenoma, papilloma, adenoma, leiomyoma, rhabdomyoma, hemangioma, lymphangioma, osteoma, chondroma, lipoma and fibroma.

36. The use of any one of claims **31** to **35**, further comprising a therapeutically effective amount of one or more additional therapeutic agents to be administered to the subject.

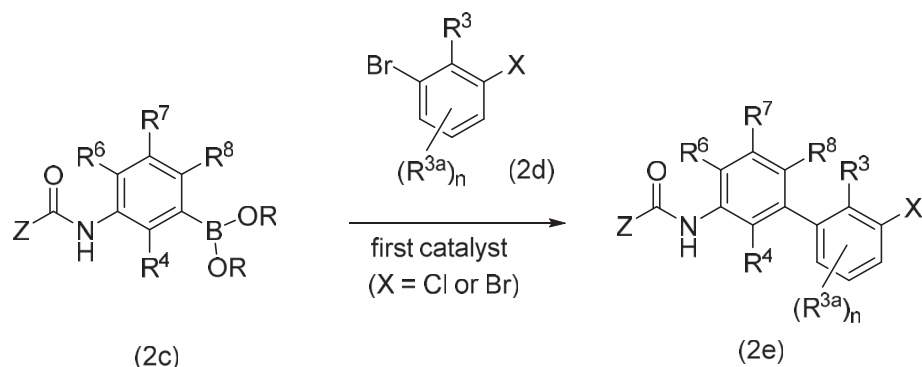
37. The use of claim **36**, wherein the one or more additional therapeutic agents is selected from the group consisting of an antimicrobial agent, an antiviral agent, a cytotoxic agent, a gene expression modulatory agent, a chemotherapeutic agent, an anti-cancer agent, an anti-angiogenic agent, an immunotherapeutic agent, an anti-hormonal agent, an anti-fibrotic agent, radiotherapy, a radiotherapeutic agent, an anti-neoplastic agent, and an anti-proliferation agent.

38. A process for preparing a compound of formula (II),

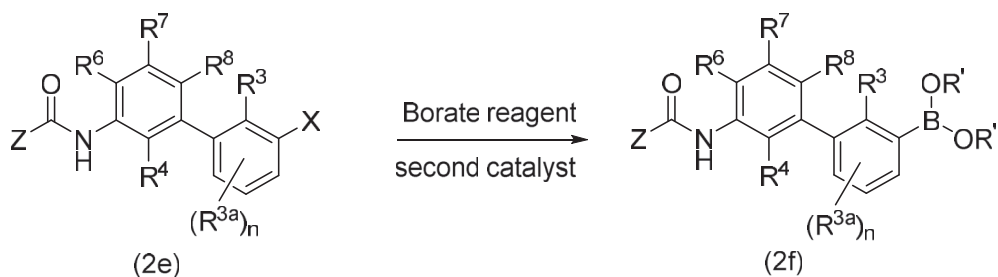


the process comprising:

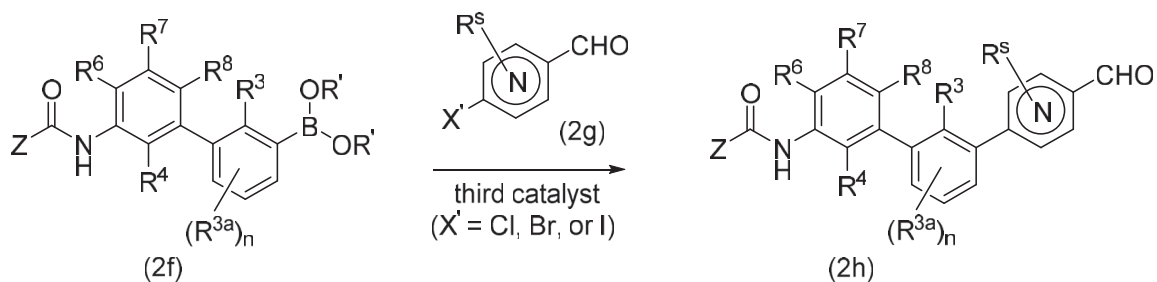
(a) contacting a compound having formula (2c) with a compound having formula (2d) and a first catalyst, under Suzuki-type conditions to produce a compound having formula (2e);



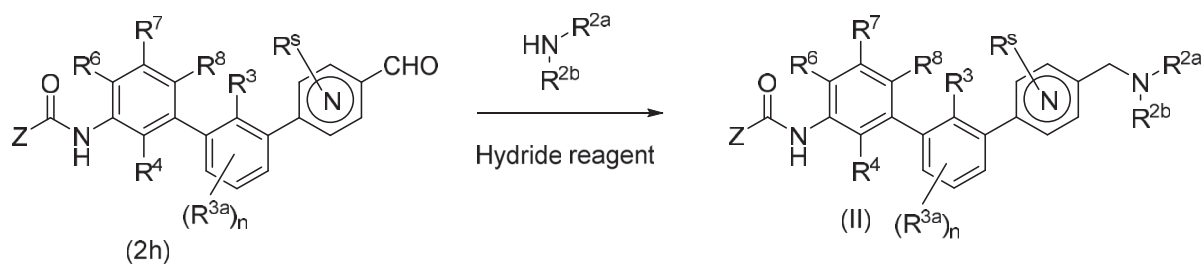
(b) converting the compound having formula (2e) to a compound having formula (2f) with a borate reagent and a second catalyst;



(c) contacting a compound having formula (2f) with a compound having formula (2g) and a third catalyst, under Suzuki-type conditions to produce a compound having formula (2h);

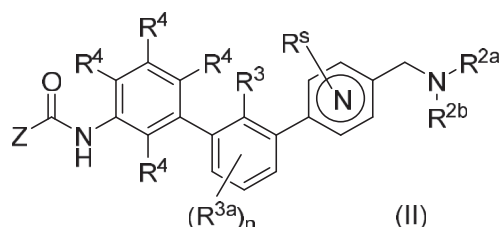


(d) reductively aminating the compound having formula (2h) with $\text{HN}(\text{R}^{2a})(\text{R}^{2b})$ and a hydride reagent to provide the compound having formula (II),



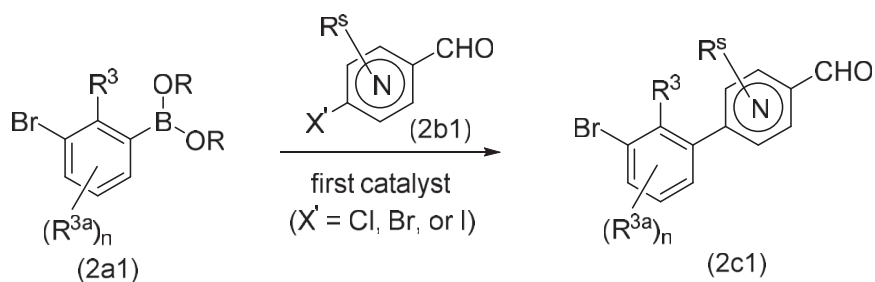
wherein in the above formulae (2c), (2d), (2e), (2f), (2h), and (II), each of Z, R^{2a}, R^{2b}, R³, R^{3a}, subscript n, R⁴, R⁵, R⁶, R⁷, R⁸, have the meanings provided in claim 1;
R and R' are each independently selected from the group consisting of H and C₁-C₆ alkyl;
X is a member selected from the group consisting of Br and Cl;
X' is a member selected from the group consisting of I, Br and Cl;
the ring bearing R^s is a six-membered nitrogen heteroaryl ring selected from the group consisting of pyridine, pyrimidine and pyrazine, and R^s is 0, 1, 2 or 3 substituents independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy, OH, and CN.

39. A process for preparing a compound of formula (II),

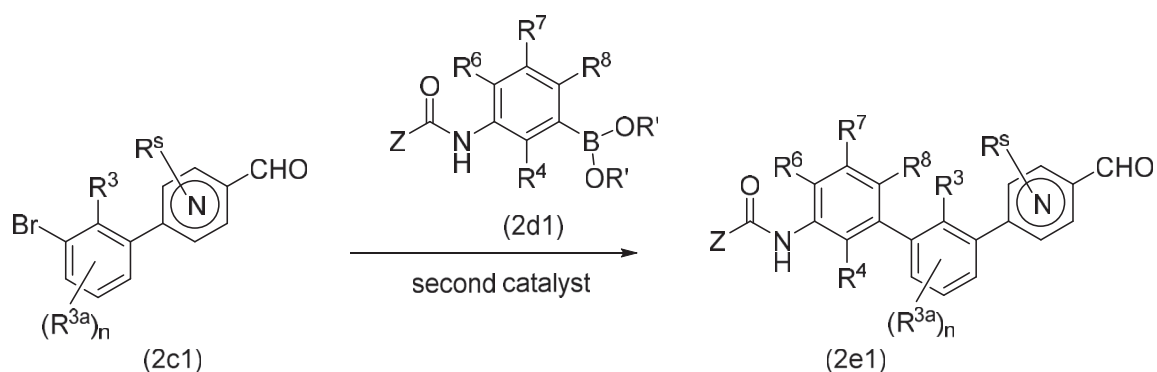


the process comprising:

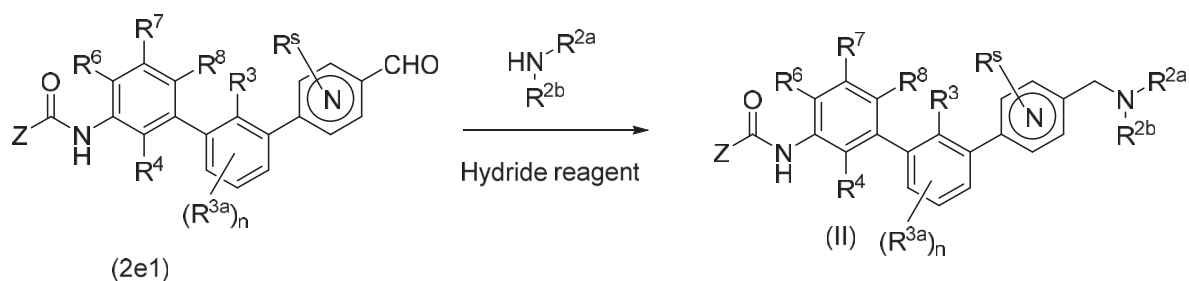
(a) contacting a compound having formula (2a1) with a compound having formula (2b1) and a first catalyst, under Suzuki-type conditions to produce a compound having formula (2c1);



(b) contacting a compound having formula (2c1) with a compound having formula (2d1) and a second catalyst, under Suzuki-type conditions to produce a compound having formula (2e1);



(c) reductively aminating the compound having formula (2e1) with $\text{HN}(\text{R}^{2a})(\text{R}^{2b})$ and a hydride reagent to provide the compound having formula (II),



wherein in the above formulae (2a1), (2b1), (2c1), (2d1), (2e1), and (II), each of Z, R^{2a} , R^{2b} ,

R^3 , R^{3a} , subscript n, R^4 , R^5 , R^6 , R^7 , R^8 , have the meanings provided in claim 1;

R and R' are each independently selected from the group consisting of H and $\text{C}_1\text{-C}_6$ alkyl;

X' is a member selected from the group consisting of I, Br and Cl;

the ring bearing R^s is a six-membered nitrogen heteroaryl ring selected from the group consisting of pyridine, pyrimidine and pyrazine, and R^s is 0, 1, 2 or 3 substituents

independently selected from the group consisting of halogen, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy, OH, and CN.