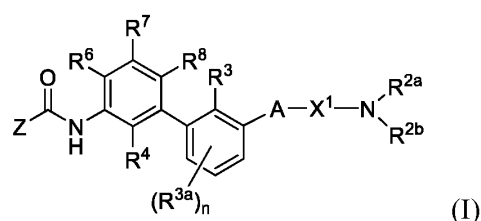


WHAT IS CLAIMED IS:

1. A compound of Formula (I):



or a pharmaceutically acceptable salt, prodrug or bioisostere thereof, wherein:

A is a 5- to 10-membered heteroaryl group which is unsubstituted or substituted with from one to five members independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy, OH, and CN;

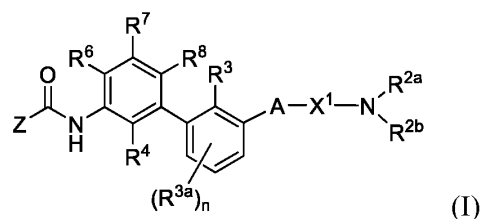
X¹ is C₁₋₃ alkylene, which is unsubstituted or substituted with one or two members independently selected from the group consisting of C₁₋₂ alkyl and CO₂H;

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 and 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, CO₂C₁₋₈ 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

24 alkyl, C₁₋₈ haloalkyl, C₁₋₈ hydroxyalkyl, -X³-CO₂R^a, -X³-OR^a, -X³-NR^aR^b,
 25 -X³-C(O)NR^aR^b, -X³-SO₂R^a, -X³-SO₂NR^aR^b, -X³-N(R^b)SO₂R^a, and -X³-SO₃R^a,
 26 wherein X³ is a bond or C₁₋₆ alkylene;
 27 R³ and R⁴ are each independently selected from the group consisting of H, F, Cl, CN, CH₃,
 28 OCH₃, CH₂CH₃ and CF₃;
 29 the subscript n is 0, 1, 2 or 3;
 30 each R^{3a} is independently selected from the group consisting of H, F, Cl, C₁₋₃ alkyl, C₁₋₃ alkoxy,
 31 C₁₋₃ haloalkyl, C₁₋₃ haloalkoxy, C₂₋₃ alkenyl and CN;
 32 R⁶, R⁷ and R⁸ are each independently selected from the group consisting of H, F, Cl, CN, CH₃,
 33 OCH₃, CH₂CH₃ and CF₃;
 34 Z is selected from the group consisting of:
 35 i) a monocyclic, bicyclic, or spirocyclic non-aromatic heterocyclic ring, optionally
 36 substituted with one or two oxo groups and optionally substituted with up to four R^a
 37 and/or R^b; and
 38 ii) a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with one to
 39 three R^c;
 40 each R^a is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆
 41 haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H;
 42 each R^b is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆
 43 haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H, each of which
 44 is unsubstituted or substituted with one or two members independently selected from OH,
 45 SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl and CO₂H;
 46 and R^a and R^b, when attached to the same nitrogen atom, are optionally combined to form a 4- to
 47 8-membered ring or spirocyclic ring, which is unsubstituted or substituted with halogen,
 48 OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl or CO₂H;
 49 each R^c is independently selected from the group consisting of H, halogen, CN, C₁₋₆ alkyl, C₁₋₆
 50 haloalkyl, -Y¹, -X⁴-CO₂R^a, -O-X⁴-CO₂R^a, -X⁴-OR^a, -X⁴-NR^aR^b, -X⁴-C(O)NR^aR^b,
 51 -O-X⁴-C(O)NR^aR^b, -X⁴-SO₂R^a, -X⁴-SO₂NR^aR^b, -X⁴-SO₃R^a, and -N(R^a)-X⁴-CO₂R^a,
 52 wherein each X⁴ is a bond or C₁₋₆ alkylene, and each Y¹ is selected from the group
 53 consisting of C₃₋₆ cycloalkyl and C₄₋₈ heterocyclyl; and optionally two R^c on adjacent ring
 54 vertices are combined to form a fused 5- or 6-membered heterocyclic ring.

2. A compound of Formula (I):



or a pharmaceutically acceptable salt, prodrug or bioisostere thereof, wherein:

A is a 5- to 10-membered heteroaryl group which is unsubstituted or substituted with from one to five members independently selected from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy and CN;

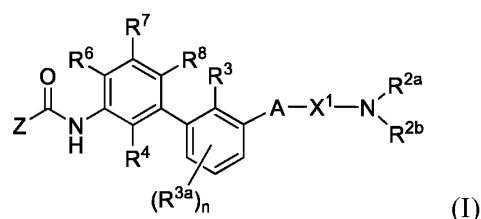
X¹ is C₁₋₃ alkylene, which is unsubstituted or substituted with one or two members independently selected from the group consisting of C₁₋₂ alkyl and CO₂H;

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 and 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, CO₂C₁₋₈ 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, -X³-C(O)NR^aR^b, -X³-SO₂R^a, -X³-SO₂NR^aR^b, -X³-N(R^b)SO₂R^a, and -X³-SO₃R^a; wherein X³ is a bond or C₁₋₆ alkylene;

27 R³ and R⁴ are each independently selected from the group consisting of F, Cl, CN, CH₃, OCH₃,
28 CH₂CH₃ and CF₃;
29 the subscript n is 0, 1, 2 or 3;
30 each R^{3a} is independently selected from the group consisting of H, F, Cl, C₁₋₃ alkyl, C₁₋₃ alkoxy,
31 C₁₋₃ haloalkyl, C₁₋₃ haloalkoxy, C₂₋₃ alkenyl and CN;
32 R⁶, R⁷ and R⁸ are each independently selected from the group consisting of H, F, Cl, CN, CH₃,
33 OCH₃, CH₂CH₃ and CF₃;
34 Z is selected from the group consisting of:
35 i) a monocyclic, bicyclic, or spirocyclic non-aromatic heterocyclic ring, optionally
36 substituted with one or two oxo groups and optionally substituted with up to four R^a
37 and/or R^b, and
38 ii) a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with one to
39 three R^c;
40 each R^a is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆
41 haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H;
42 each R^b is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆
43 haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H, each of which
44 is unsubstituted or substituted with one or two members independently selected from OH,
45 SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl and CO₂H;
46 and R^a and R^b, when attached to the same nitrogen atom, are optionally combined to form a 4- to
47 8-membered ring or spirocyclic ring, which is unsubstituted or substituted with halogen,
48 OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl or CO₂H;
49 each R^c is independently selected from the group consisting of H, halogen, CN, C₁₋₆ alkyl, C₁₋₆
50 haloalkyl, -Y¹, -X⁴-CO₂R^a, -O-X⁴-CO₂R^a, -X⁴-OR^a, -X⁴-NR^aR^b, -X⁴-C(O)NR^aR^b,
51 -O-X⁴-C(O)NR^aR^b, -X⁴-SO₂R^a, -X⁴-SO₂NR^aR^b, -X⁴-SO₃R^a, and -N(R^a)-X⁴-CO₂R^a,
52 wherein each X⁴ is a bond or C₁₋₆ alkylene, and each Y¹ is selected from the group
53 consisting of C₃₋₆ cycloalkyl and C₄₋₈ heterocyclyl; and optionally two R^c on adjacent ring
54 vertices are combined to form a fused 5- or 6-membered heterocyclic ring..

1 **3.** A compound of Formula (I):



2

3 or a pharmaceutically acceptable salt, prodrug or bioisostere thereof, wherein:

4 A is a 5- to 10-membered heteroaryl group which is unsubstituted or substituted with from one to
 5 five members independently selected from the group consisting of halogen, C₁₋₃ alkyl,
 6 C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy and CN;

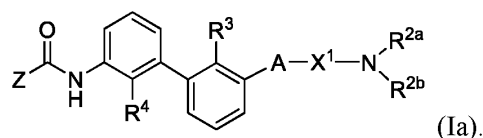
7 X¹ is C₁₋₃ alkylene, which is unsubstituted or substituted with one or two members independently
 8 selected from the group consisting of C₁₋₂ alkyl and CO₂H;

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

20 or R^{2a} and R^{2b} are combined to form a 4- to 9-membered ring or spirocyclic ring, having from
 21 zero to two additional heteroatom ring vertices selected from O, N or S;
 22 wherein the ring formed by combining R^{2a} and R^{2b}, is unsubstituted or substituted with 1
 23 to 4 substituents independently selected from the group consisting of oxo, C₁₋₈
 24 alkyl, C₁₋₈ haloalkyl, C₁₋₈ hydroxyalkyl, -X³-CO₂R^a, -X³-OR^a, -X³-NR^aR^b,
 25 -X³-C(O)NR^aR^b, -X³-SO₂R^a, -X³-SO₂NR^aR^b, and -X³-SO₃R^a, wherein X³ is a
 26 bond or C₁₋₆ alkylene;

27 R³ and R⁴ are each independently selected from the group consisting of F, Cl, CN, CH₃, OCH₃,
28 CH₂CH₃ and CF₃;
29 the subscript n is 0, 1, 2 or 3;
30 each R^{3a} is independently selected from the group consisting of H, F, Cl, C₁₋₃ alkyl, C₁₋₃ alkoxy,
31 C₁₋₃ haloalkyl, C₁₋₃ haloalkoxy, C₂₋₃ alkenyl and CN;
32 R⁶, R⁷ and R⁸ are each independently selected from the group consisting of H, F, Cl, CN, CH₃,
33 OCH₃, CH₂CH₃ and CF₃;
34 Z is selected from the group consisting of:
35 i) a monocyclic, bicyclic, or spirocyclic non-aromatic heterocyclic ring, optionally
36 substituted with one or two oxo groups and optionally substituted with up to four R^a
37 and/or R^b, and
38 ii) a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with one to
39 three R^c;
40 each R^a is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆
41 haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H;
42 each R^b is independently selected from the group consisting of H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆
43 haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkylene-CO₂H, and C₁₋₆ alkylene-SO₃H, each of which
44 is unsubstituted or substituted with one or two members independently selected from OH,
45 SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl and CO₂H;
46 and R^a and R^b, when attached to the same nitrogen atom, are optionally combined to form a 4- to
47 8-membered ring or spirocyclic ring, which is unsubstituted or substituted with halogen,
48 OH, SO₂NH₂, C(O)NH₂, C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl or CO₂H;
49 each R^c is independently selected from the group consisting of H, halogen, CN, C₁₋₆ alkyl, C₁₋₆
50 haloalkyl, -Y¹, -X⁴-CO₂R^a, -O-X⁴-CO₂R^a, -X⁴-OR^a, -X⁴-NR^aR^b, -X⁴-C(O)NR^aR^b,
51 -O-X⁴-C(O)NR^aR^b, -X⁴-SO₂R^a, -X⁴-SO₂NR^aR^b, -X⁴-SO₃R^a, and -N(R^a)-X⁴-CO₂R^a,
52 wherein each X⁴ is a bond or C₁₋₆ alkylene, and each Y¹ is selected from the group
53 consisting of C₃₋₆ cycloalkyl and C₄₋₈ heterocyclyl; and optionally two R^c on adjacent ring
54 vertices are combined to form a fused 5- or 6-membered heterocyclic ring.

1 4. The compound of claim 1 or claim 3, or a pharmaceutically acceptable salt
2 thereof having formula (Ia):

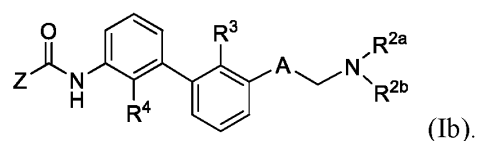


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1 5. The compound of any one of claims 1 to 4, or a pharmaceutically
2 acceptable salt thereof wherein A is a 5- or 6-membered heteroaryl group which is unsubstituted
3 or substituted with from one to three members independently selected from the group consisting
4 of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, OH, and CN.

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

1 7. The compound of any one of claims 1 to 6 a pharmaceutically acceptable
2 salt thereof having formula (Ib):

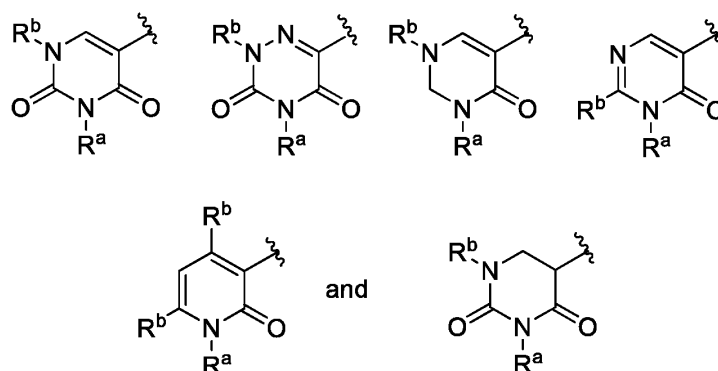


3

1 8. The compound of any one of claims 1 to 7, or a pharmaceutically
2 acceptable salt thereof wherein A is unsubstituted or substituted with one or two members
3 independently selected from the group consisting of CF₃, OH, Et, CN, OCH₃ and F.

1 9. The compound of any one of claims 1 to 7, or a pharmaceutically
2 acceptable salt thereof wherein A is a 6-membered heteroaryl selected from the group consisting
3 of pyridine, pyrimidine, pyrazine and 1,2,4-triazine, each of which is unsubstituted or substituted
4 with one or two members independently selected from the group consisting of CF₃, OH, Et, CN,
5 OCH₃ and F.

1 10. The compound of any one of claims 1 to 7, or a pharmaceutically
2 acceptable salt thereof wherein Z is a non-aromatic heterocyclic ring having a formula selected
3 from the group consisting of:

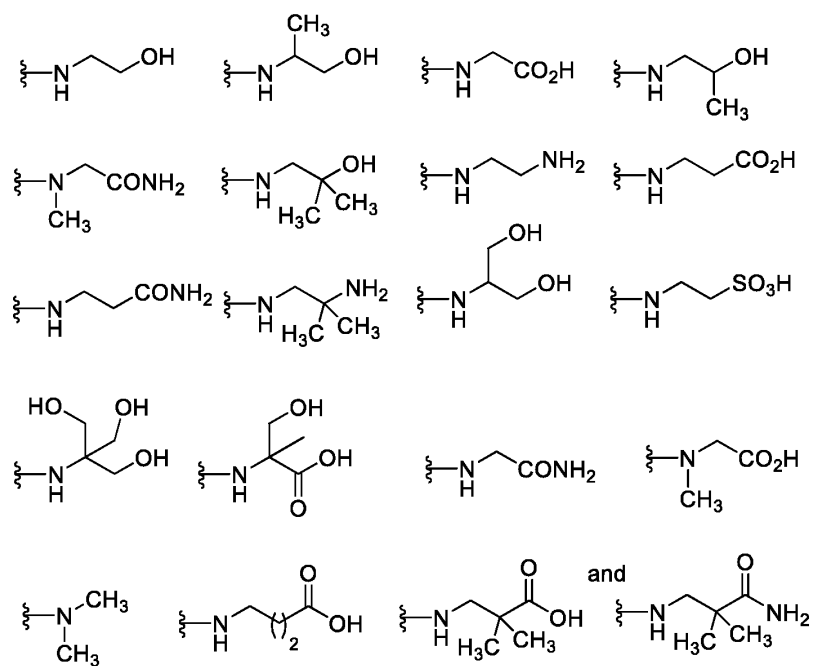


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1 **11.** The compound of any one of claims **1** to **7**, or a pharmaceutically
 2 acceptable salt thereof wherein Z is a monocyclic 5- or 6-membered heteroaryl ring, optionally
 3 substituted with one to three R^c ; and said heterocyclic ring is selected from the group consisting
 4 of pyridinyl, pyrimidinyl, pyrazinyl, oxazolyl, thiazolyl, and pyrazolyl.

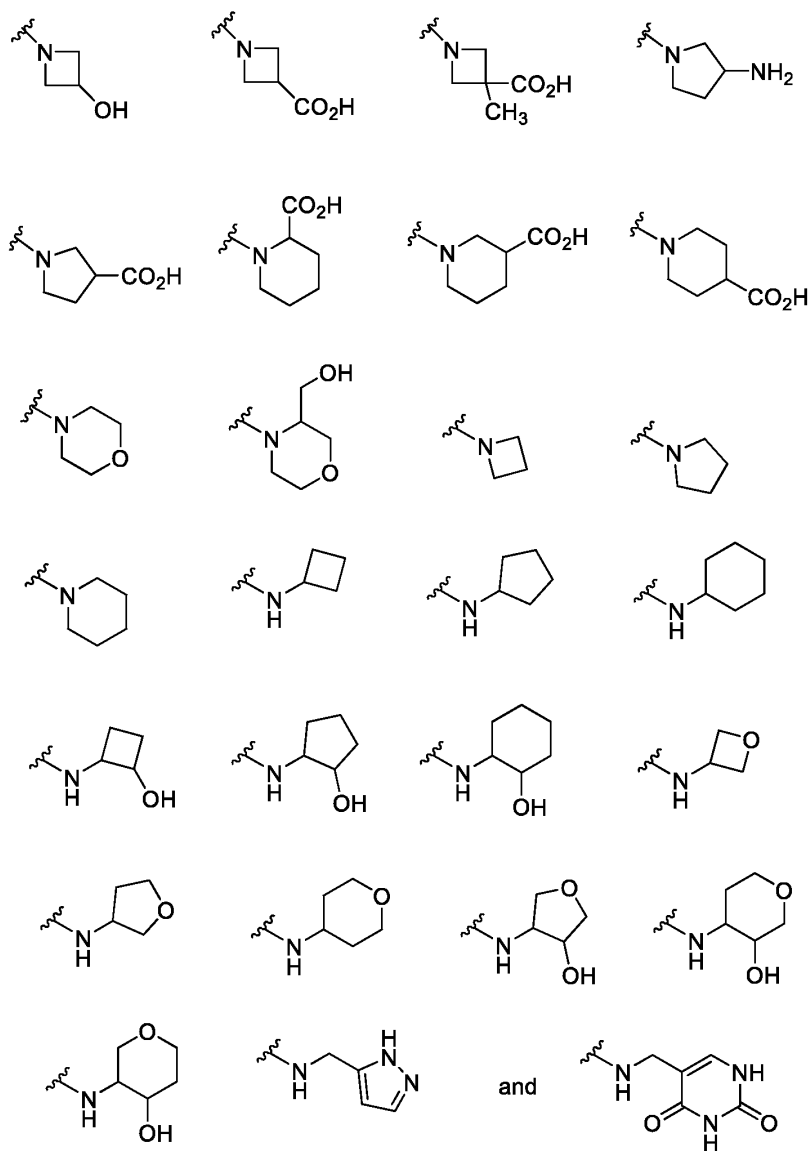
1 **12.** The compound of any one of claims **1** to **7**, or a pharmaceutically
 2 acceptable salt thereof, wherein Z is a non-aromatic heterocyclic ring selected from the group
 3 consisting of piperidinyl, morpholinyl, tetrahydropyranyl, and tetrahydrofuranyl, each of which
 4 is optionally substituted with up to four R^a and/or R^b .

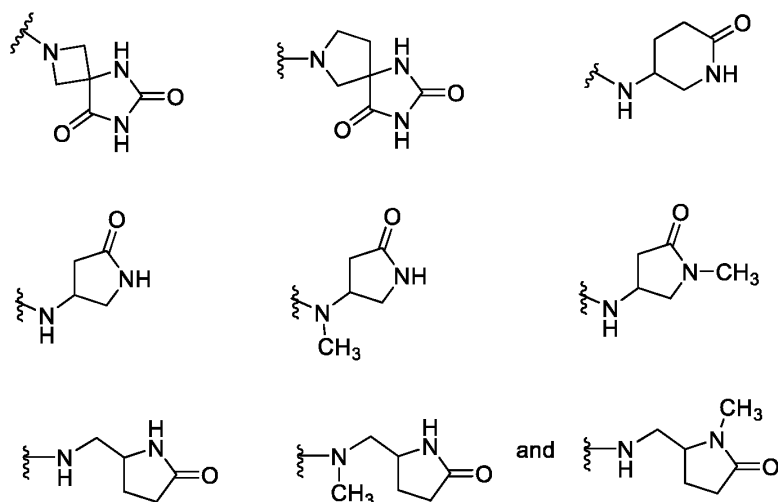
1 **13.** The compound of any one of claims **1** to **11**, or a pharmaceutically
 2 acceptable salt thereof wherein $-N(R^{2a})(R^{2b})$ is selected from the group consisting of:



3

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





3

1 **16.** The compound of any one of claims **1** to **15**, or a pharmaceutically
2 acceptable salt thereof, wherein the compound is an optically pure or enriched isomer.

1 **17.** The compound of any one of claims **1** to **15**, or a pharmaceutically
2 acceptable salt thereof wherein Y is selected from the group consisting of C₃₋₆ cycloalkyl and C₄₋₈
3 heterocyclyl, each of which is unsubstituted or substituted with one to four substituents
4 independently selected from the group consisting of oxo, OH, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄
5 hydroxyalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₁₋₄ hydroxyalkoxy, SO₂NH₂, C(O)NH₂,
6 C(O)NHOH, PO₃H₂, CO₂C₁₋₈ alkyl, SO₃H and CO₂H.

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

1 **19.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof
2 wherein Z is a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with one to
3 three R^c.

1 **20.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof
2 wherein Z is a 5- or 6-membered monocyclic non-aromatic heterocyclic ring, optionally

3 substituted with one or two oxo groups and optionally substituted with R^a and/or R^b; and each of
4 R⁶, R⁷ and R⁸ is H.

1 **21.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof
2 wherein Z is a monocyclic 5- or 6-membered heteroaryl ring, optionally substituted with one to
3 three R^c; and each of R⁶, R⁷ and R⁸ is H.

1 **22.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof
2 wherein Z is a 5- or 6-membered non-aromatic heterocyclic ring selected from the group
3 consisting of piperidinyl, morpholinyl, tetrahydropyranyl, and tetrahydrofuranyl, optionally
4 substituted with one or two oxo groups and optionally substituted with R^a and/or R^b.

1 **23.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof
2 wherein Z is a monocyclic 5- or 6-membered heteroaryl ring selected from the group consisting
3 of pyridinyl, pyrimidinyl, pyrazinyl, oxazolyl, thiazolyl, and pyrazolyl, each of which is
4 optionally substituted with one to three R^c.

1 **24.** The compound of claim **1**, wherein said compound is selected from the
2 compounds in Table 1.

1 **25.** A pharmaceutical composition comprising a compound of any one of
2 claims **1** to **24**, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable
3 excipient.

1 **26.** The pharmaceutical composition of claim **25**, further comprising one or
2 more additional therapeutic agents.

1 **27.** The pharmaceutical composition of claim **26**, wherein the one or more
2 additional therapeutic agent is selected from the group consisting of an antimicrobial agent, an
3 antiviral agent, a cytotoxic agent, a gene expression modulatory agent, a chemotherapeutic agent,
4 an anti-cancer agent, an anti-angiogenic agent, an immunotherapeutic agent, an anti-hormonal
5 agent, an anti-fibrotic agent, radiotherapy, a radiotherapeutic agent, an anti-neoplastic agent, and
6 an anti-proliferation agent.

1 **28.** A method of modulating an immune response mediated by the PD-1
2 signaling pathway in a subject, comprising administering to the subject a therapeutically
3 effective amount of a compound of any one of claims **1** to **24**, or a pharmaceutically acceptable
4 salt thereof or a composition of any one of claims **25** to **27**.

1 **29.** A method of enhancing, stimulating, modulating and/or increasing the
2 immune response in a subject in need thereof, comprising administering to the subject a
3 therapeutically effective amount of a compound of any one of claims **1** to **24**, or a
4 pharmaceutically acceptable salt thereof or a composition of any one of claims **25** to **27**.

1 **30.** A method of inhibiting growth, proliferation, or metastasis of cancer cells
2 in a subject in need thereof, comprising administering to the subject a therapeutically effective
3 amount of a compound of any one of claims **1** to **24**, or a pharmaceutically acceptable salt
4 thereof or a composition of any one of claims **25** to **27**.

1 **31.** A method of treating a subject suffering from or susceptible to a disease or
2 disorder mediated by the PD-1 signaling pathway, comprising administering to the subject a
3 therapeutically effective amount of a compound of any one of claims **1** to **24**, or a
4 pharmaceutically acceptable salt thereof or a composition of any one of claims **25** to **27**.

1 **32.** The method of any one of claims **28** to **31**, wherein the subject suffers
2 from a disease or disorder selected from the group consisting of an infectious disease, a bacterial
3 infectious disease, a viral infectious disease, a fungal infectious disease, a solid tumor, a
4 hematological malignancy, an immune disorder, an inflammatory disease, and cancer.

1 **33.** The method of claim **31**, wherein the disease or disorder is selected from
2 the group consisting of melanoma, glioblastoma, esophagus tumor, nasopharyngeal carcinoma,
3 uvea melanoma, lymphoma, lymphocytic lymphoma, primary CNS lymphoma, T-cell
4 lymphoma, diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, prostate
5 cancer, castration-resistant prostate cancer, chronic myelocytic leukemia, Kaposi's sarcoma
6 fibrosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, angiosarcoma,
7 lymphangiosarcoma, synovioma, , meningioma, leiomyosarcoma, rhabdomyosarcoma, sarcoma

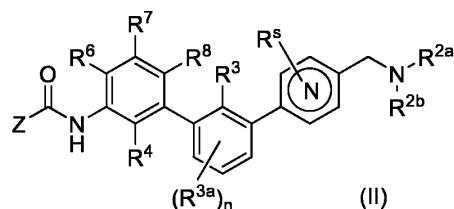
8 of soft tissue, sarcoma, sepsis, biliary tumor, basal cell carcinoma, thymus neoplasm, cancer of
9 the thyroid gland, cancer of the parathyroid gland, uterine cancer, cancer of the adrenal gland,
10 liver infection, Merkel cell carcinoma, nerve tumor, follicle center lymphoma, colon cancer,
11 Hodgkin's disease, non-Hodgkin's lymphoma, leukemia, chronic or acute leukemias including
12 acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic
13 lymphocytic leukemia, multiple myeloma, ovary tumor, myelodysplastic syndrome, cutaneous or
14 intraocular malignant melanoma, renal cell carcinoma, small-cell lung cancer, lung cancer,
15 mesothelioma, breast cancer, squamous non-small cell lung cancer (SCLC), non-squamous
16 NSCLC, colorectal cancer, ovarian cancer, gastric cancer, hepatocellular carcinoma, pancreatic
17 carcinoma, pancreatic cancer, Pancreatic ductal adenocarcinoma, squamous cell carcinoma of the
18 head and neck, cancer of the head or neck, gastrointestinal tract, stomach cancer, HIV, Hepatitis
19 A, Hepatitis B, Hepatitis C, Hepatitis D, herpes viruses, papillomaviruses, influenza, bone
20 cancer, skin cancer, rectal cancer, cancer of the anal region, testicular cancer, carcinoma of the
21 fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the
22 vagina, carcinoma of the vulva, cancer of the esophagus, cancer of the small intestine, cancer of
23 the endocrine system, cancer of the urethra, cancer of the penis, cancer of the bladder, cancer of
24 the kidney, cancer of the ureter, carcinoma of the renal pelvis, neoplasm of the central nervous
25 system (CNS), tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma,
26 epidermoid cancer, abestosis, carcinoma, adenocarcinoma, papillary carcinoma,
27 cystadenocarcinoma, bronchogenic carcinoma, renal cell carcinoma, transitional cell carcinoma,
28 choriocarcinoma, seminoma, embryonal carcinoma, wilm's tumor, pleomorphic adenoma, liver
29 cell papilloma, renal tubular adenoma, cystadenoma, papilloma, adenoma, leiomyoma,
30 rhabdomyoma, hemangioma, lymphangioma, osteoma, chondroma, lipoma and fibroma.

1 **34.** The method of any one of claims **28** to **33**, further comprising
2 administering to the subject a therapeutically effective amount of one or more additional
3 therapeutic agents.

1 **35.** The method of claim **34**, wherein the one or more additional therapeutic
2 agents is selected from the group consisting of an antimicrobial agent, an antiviral agent, a
3 cytotoxic agent, a gene expression modulatory agent, a chemotherapeutic agent, an anti-cancer
4 agent, an anti-angiogenic agent, an immunotherapeutic agent, an anti-hormonal agent, an anti-

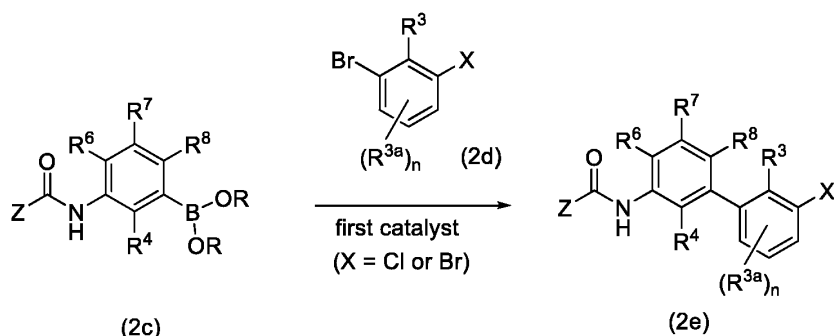
5 fibrotic agent, radiotherapy, a radiotherapeutic agent, an anti-neoplastic agent, and an anti-
6 proliferation agent.

1 **36.** A process for preparing a compound of formula (II),

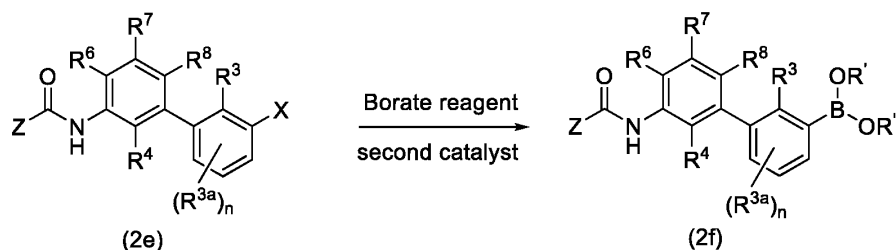


2
3 the process comprising:

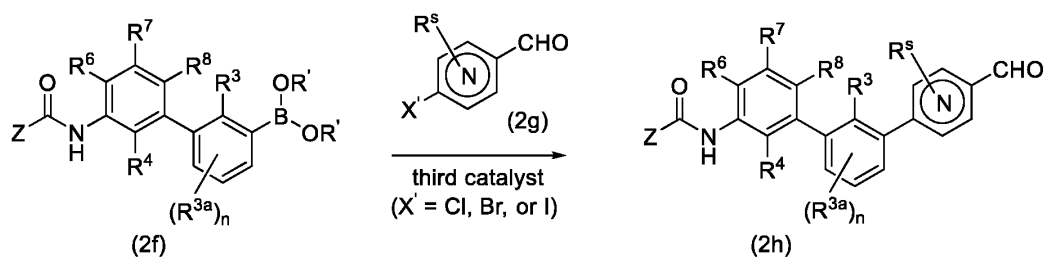
(a) contacting a compound having formula (2c) with a compound having formula (2d) and a first catalyst, under Suzuki-type conditions to produce a compound having formula (2e);



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

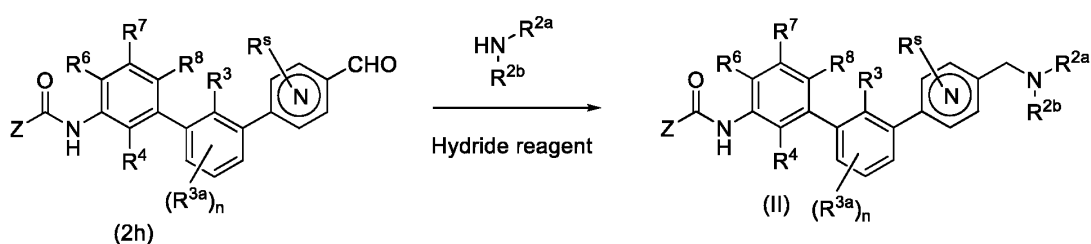


10 (c) contacting a compound having formula (2f) with a compound having formula (2g)
11 and a third catalyst, under Suzuki-type conditions to produce a compound having formula (2h);



12

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



15

16 wherein in the above formulae (2c), (2d), (2e), (2f), (2h), and (II), each of Z, R^{2a} , R^{2b} , R^3 , R^{3a} ,
 17 subscript n, R^4 , R^5 , R^6 , R^7 , R^8 , have the meanings provided in claim 1;

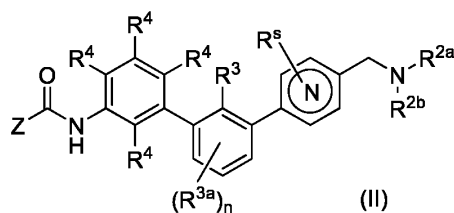
18 R and R' are each independently selected from the group consisting of H and $\text{C}_1\text{-C}_6$ alkyl;

19 X is a member selected from the group consisting of Br and Cl;

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

21 the ring bearing R^5 is a six-membered nitrogen heteroaryl ring selected from the group consisting
 22 of pyridine, pyrimidine and pyrazine, and R^5 is 0, 1, 2 or 3 substituents independently selected
 23 from the group consisting of halogen, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy,
 24 OH, and CN.

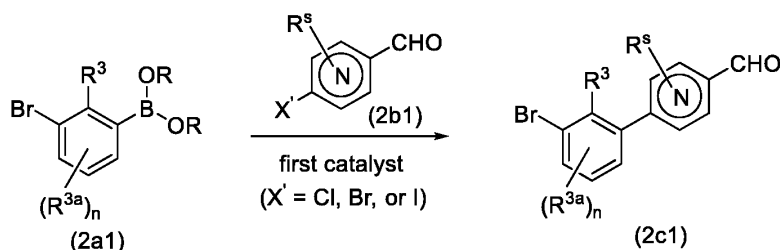
1 37. A process for preparing a compound of formula (II),



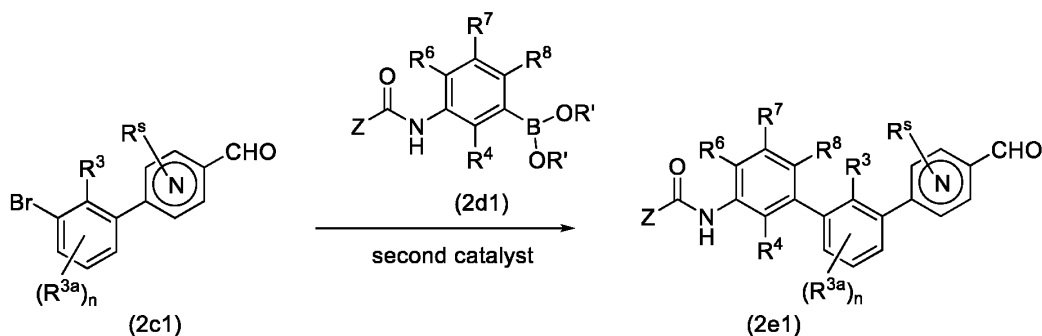
2

3 the process comprising:

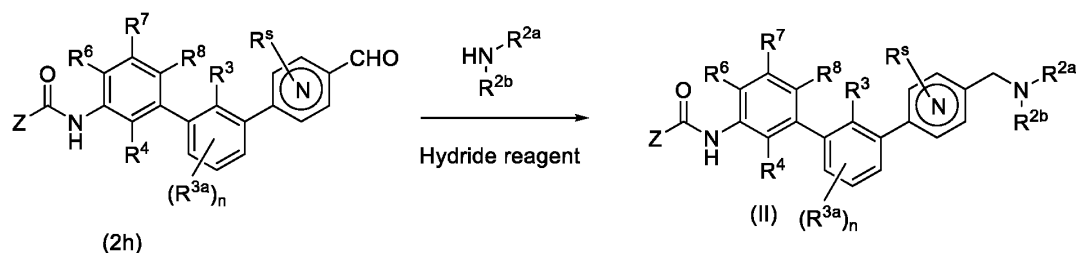
- 4 (a) contacting a compound having formula (2a1) with a compound having formula (2b1)
 5 and a first catalyst, under Suzuki-type conditions to produce a compound having formula (2c1);



- 6
 7 (b) contacting a compound having formula (2c1) with a compound having formula (2d1)
 8 and a second catalyst, under Suzuki-type conditions to produce a compound having formula
 9 (2e1);



- 10
 11 (c) reductively aminating the compound having formula (2e1) with $\text{HN(R}^{2a}\text{)(R}^{2b}\text{)}$ and a
 12 hydride reagent to provide the compound having formula (II),



- 13
 14 wherein in the above formulae (2a1), (2b1), (2c1), (2d1), (2e1), and (II), each of Z, R^{2a} ,
 15 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;
 16 **R and R' are each independently selected from the group consisting of H and C₁-C₆ alkyl;**
 17 **X' is a member selected from the group consisting of I, Br and Cl;**

18 the ring bearing R^s is a six-membered nitrogen heteroaryl ring selected from the group consisting
19 of pyridine, pyrimidine and pyrazine, and R^s is 0, 1, 2 or 3 substituents independently selected
20 from the group consisting of halogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy,
21 OH, and CN.