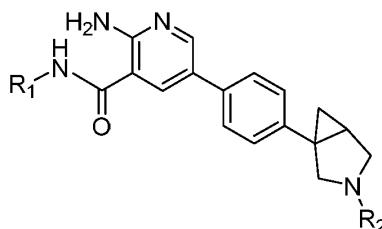


CLAIMS

1. A compound of Formula I:



(I)

5

or a pharmaceutically acceptable salt thereof;
wherein

R₁ is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C₁-C₃ alkoxy;

- 10 R₂ is selected from the group consisting of C₁-C₃ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₁-C₃ alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R³; and

R³ is selected from the group consisting of hydroxy, halo, cyano, nitro, SO₂-C₁-C₃ alkyl, and SO₃H;

- 15 for use in the treatment of anemia in a subject in need thereof.

2. The compound for use of claim 1, wherein R₁ is bridged C₈-cycloalkyl substituted with hydroxy.

- 20 3. The compound for use of claim 1 or 2, wherein R₂ is tetrahydropyran.

4. The compound for use of any one of claims 1-3, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-(3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.

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5. The compound for use of claim 4, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1R,5S)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.

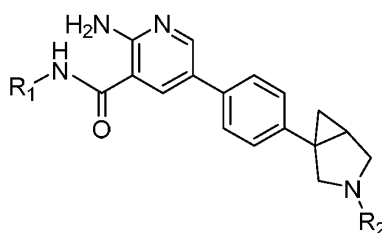
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6. The compound for use of claim 4, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1S,5R)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.
- 5 7. The compound for use of any one of claims 1-6, wherein the subject suffers from a myelodysplastic syndrome (MDS).
8. The compound for use of claim 7, wherein the myelodysplastic syndrome (MDS) is
10 selected from the group consisting of MDS with multilineage dysplasia (MDS-MLD), MDS with single lineage dysplasia (MDS-SLD), MDS with excess blasts (MDS-EB), MDS with isolated del(5q), and MDS unclassifiable (MDS-U).
9. The compound for use of any one of claims 1-6, wherein the subject suffers from
15 multiple myeloma (MM).
10. The compound for use of any one of claims 1-6, wherein the subject suffers from myelofibrosis (MF).
- 20 11. The compound for use of any one of claims 1-6, wherein the anemia is iron-refractory iron deficiency anemia (IRIDA).
12. The compound for use of any one of claims 1-11, wherein the subject is transfusion-dependent.
25
13. The compound for use of any one of claims 1-11, wherein the subject is not transfusion-dependent.
14. The compound for use of any one of claims 1-13, wherein the compound of Formula I
30 is administered orally.
15. The compound for use of any one of claims 1-14, wherein the compound of Formula I is administered as a monotherapy for anemia treatment.
- 35 16. The compound for use of any one of claims 1-15, wherein the compound of Formula I is administered at a dose of about 5 mg to about 500 mg once daily (QD).

17. The compound for use of any one of claims 1-16, wherein the compound of Formula I is administered at a dose of about 50 mg once daily (QD).

18. The compound for use of any one of claims 1-17, wherein the compound of Formula I is administered as a 5 mg, 25 mg, or 50 mg tablet, or a combination thereof.

19. A compound of Formula I:



(I)

10 or a pharmaceutically acceptable salt thereof;
wherein

R₁ is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C₁-C₃ alkoxy;

15 R₂ is selected from the group consisting of C₁-C₃ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₁-C₃ alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R³; and

R³ is selected from the group consisting of hydroxy, halo, cyano, nitro, SO₂-C₁-C₃ alkyl, and SO₃H;

for use in reducing hepcidin levels in a subject in need thereof.

20

20. The compound for use of claim 19, wherein R₁ is bridged C₈-cycloalkyl substituted with hydroxy.

21. The compound for use of claim 19 or 20, wherein R₂ is tetrahydropyran.

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22. The compound for use of any one of claims 19-21, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-(3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.

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23. The compound for use of claim 22, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1R,5S)-3-(tetrahydro-2H-pyran-4-yl)-3-

azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.

24. The compound for use of claim 22, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1S,5R)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.

25. The compound for use of any one of claims 19-24, wherein the subject suffers from anemia.

26. The compound for use of claim 25, wherein the anemia is iron-refractory iron deficiency anemia (IRIDA).

27. The compound for use of any one of claims 19-26, wherein the subject is transfusion-dependent.

28. The compound for use of any one of claims 19-26, wherein the subject is not transfusion-dependent.

29. The compound for use of any one of claims 19-28, wherein the subject suffers from a myelodysplastic syndrome (MDS).

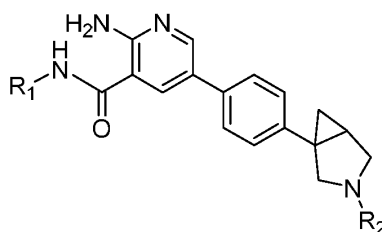
30. The compound for use of claim 29, wherein the myelodysplastic syndrome (MDS) is selected from the group consisting of MDS with multilineage dysplasia (MDS-MLD), MDS with single lineage dysplasia (MDS-SLD), MDS with excess blasts (MDS-EB), MDS with isolated del(5q), and MDS unclassifiable (MDS-U).

31. The compound for use of any one of claims 19-28, wherein the subject suffers from multiple myeloma (MM).

32. The compound for use of any one of claims 19-28, wherein the subject suffers from myelofibrosis (MF).

33. The compound for use of any one of claims 19-32, wherein the compound of Formula I is administered orally.

34. The compound for use of any one of claims 19-33, wherein the compound of Formula I is administered as a monotherapy to reduce hepcidin levels.
35. The compound for use of any one of claims 19-34, wherein the compound of Formula I is administered at a dose of about 5 mg to about 500 mg once daily (QD).
36. The compound for use of any one of claims 19-35, wherein the compound of Formula I is administered at a dose of about 50 mg once daily (QD).
37. The compound for use of any one of claims 19-36, wherein the compound of Formula I is administered as a 5 mg, 25 mg, or 50 mg tablet, or a combination thereof.
38. A compound of Formula I:



(I)

- or a pharmaceutically acceptable salt thereof;
wherein
R₁ is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C₁-C₃ alkoxy;
R₂ is selected from the group consisting of C₁-C₃ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₁-C₃ alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R³; and
R³ is selected from the group consisting of hydroxy, halo, cyano, nitro, SO₂-C₁-C₃ alkyl, and SO₃H;
for use in the treatment of chronic kidney disease (CKD)-induced anemia in a subject in need thereof.
39. The compound for use of claim 38, wherein R₁ is bridged C₈-cycloalkyl substituted with hydroxy.
40. The compound for use of claim 38 or 39, wherein R₂ is tetrahydropyran.

41. The compound for use of any one of claims 38-40, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-(3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.
- 5
42. The compound for use of claim 41, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo-[2.2.2]octan-1-yl)-5-(4-((1R,5S)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo-[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.
- 10
43. The compound for use of claim 41, wherein the compound of Formula I is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1S,5R)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.
- 15
44. The compound for use of any one of claims 38-43, wherein the compound of Formula I is administered orally.
45. The compound for use of any one of claims 38-44, wherein the compound of Formula I is administered as a monotherapy to treat chronic kidney disease (CKD)-induced anemia.
- 20
46. The compound for use of any one of claims 38-45, wherein the compound of Formula I is administered at a dose of about 5 mg to about 500 mg once daily (QD).
47. The compound for use of any one of claims 38-45, wherein the compound of Formula I is administered at a dose of about 50 mg once daily (QD).
- 25
48. The compound for use of any one of claims 38-47, wherein the compound of Formula I is administered as a 5 mg, 25 mg, or 50 mg tablet, or a combination thereof.