CLAIMS

1. A combination therapy comprising an ALK2 inhibitor that 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, and a JAK2 inhibitor that is 3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof;

for use in the treatment of cancer in a subject in need thereof.

2. The combination therapy of claim 1, wherein the JAK2 inhibitor is (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof.

3. The combination therapy of claim 1 or 2, wherein the ALK2 inhibitor 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.

4. The combination therapy of claim 1 or 2, wherein the ALK2 inhibitor 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. The combination therapy of any one of claims 1-4, wherein the ALK2 inhibitor and JAK2 inhibitor are to be administered in a single formulation.

6. The combination therapy of claim 5, further comprising a pharmaceutically acceptable carrier.

7. The combination therapy of any one of claims 1-4, wherein the ALK2 inhibitor and JAK2 inhibitor are to be administered separately.

8. The combination therapy of any one of claims 1-7, wherein the cancer is a myeloproliferative neoplasm or a myelodysplastic syndrome.

9. The combination therapy of claim 8, wherein the cancer is selected from the group consisting of chronic myeloid leukemia (CML), polycythemia vera (PV), essential thrombocythemia (ET), myelofibrosis (MF), chronic neutrophilic leukemia, chronic eosinophilic leukemia, chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia,

hypereosinophilic syndrome, systemic mastocytosis, atypical chronic myelogenous leukemia, acute lymphoblastic leukemia (ALL), and acute myeloid leukemia (AML).

10. The combination therapy of claim 8 or 9, wherein the cancer is myelofibrosis (MF).

11. The combination therapy of any one of claims 8-10, wherein the cancer is selected from the group consisting of primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis.

12. The combination therapy of any one of claims 1-11, wherein the subject is human.

13. The combination therapy of any one of claims 1-12, wherein the treatment comprises the ALK2 inhibitor and the JAK2 inhibitor to be administered at substantially the same time.

14. The combination therapy of any one of claims 1-4 and 7-12, wherein the treatment comprises the ALK2 inhibitor and the JAK2 inhibitor to be administered at different times.

15. The combination therapy of claim 14, wherein the ALK2 inhibitor is to be administered to the subject, followed by the JAK2 inhibitor to be administered to the subject.

16. The combination therapy of claim 14, wherein the JAK2 inhibitor is to be administered to the subject, followed by the ALK2 inhibitor to be administered to the subject.

17. The combination therapy of any one of claims 1-16, wherein the ALK2 inhibitor and/or the JAK2 inhibitor are to be administered at dosages that would not be effective when one or both of the ALK2 inhibitor and the JAK2 inhibitor are to be administered alone, but which amounts are effective in combination.

18. A combination therapy comprising 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 and (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or pharmaceutically acceptable salts thereof, for use in the treatment of cancer in a subject in need thereof.

19. A pharmaceutical combination comprising

(i) a JAK2 inhibitor that is 3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof;

(ii) an ALK2 inhibitor that 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.

20. The pharmaceutical combination of claim 19, wherein the JAK2 inhibitor is (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof.

21. The pharmaceutical combination of any one of claims 19-20, wherein the ALK2 inhibitor 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.

22. The pharmaceutical combination of any one of claims 19-20, wherein the ALK2 inhibitor 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.

23. A pharmaceutical composition comprising an ALK2 inhibitor that 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, a pharmaceutically acceptable carrier, and a JAK2 inhibitor that is 3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof.

24. The pharmaceutical composition of claim 23, wherein the JAK2 inhibitor is (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof.

25. The pharmaceutical composition of claim 23, wherein the ALK2 inhibitor 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.

26. The pharmaceutical composition of claim 23, wherein the ALK2 inhibitor 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.

27. Use of a JAK2 inhibitor that is 3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof;

and an ALK2 inhibitor that 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;

in the preparation of a medicament for the treatment of myelofibrosis (MF)-induced anemia in a subject.

28. The use of claim 27, wherein

the JAK2 inhibitor is 3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof; and

the ALK2 inhibitor 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 or hydrate thereof.

29. Use of an ALK2 inhibitor that 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 pharmaceutically acceptable salt thereof, and a JAK2 inhibitor that is 3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt thereof; in the preparation of a medicament for a combination therapy in the treatment of cancer in a subject.

30. The use of claim 29, wherein the cancer is a myeloproliferative neoplasm or a myelodysplastic syndrome.

31. The use of claim 29, wherein the cancer is selected from the group consisting of chronic myeloid leukemia (CML), polycythemia vera (PV), essential thrombocythemia (ET), myelofibrosis (MF), chronic neutrophilic leukemia, chronic eosinophilic leukemia, chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia, hypereosinophilic syndrome, systemic mastocytosis, atypical chronic myelogenous leukemia, acute lymphoblastic leukemia (ALL), and acute myeloid leukemia (AML).

32. Use of 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 and (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or pharmaceutically

acceptable salts thereof, in the preparation of a medicament for a combination therapy in the treatment of cancer in a subject.

33. The combination of any one of claims 1-18, wherein the ALK2 inhibitor 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 fumarate dihydrate.

34. The combination of any one of claims 1-18, wherein the JAK2 inhibitor is (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile phosphoric acid salt.

35. The pharmaceutical combination of any one of claims 19-22, wherein the ALK2 inhibitor 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 fumarate dihydrate.

36. The pharmaceutical combination of any one of claims 19-22, wherein the JAK2 inhibitor is (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile phosphoric acid salt.

37. The pharmaceutical composition of any one of claims 23-26, wherein the ALK2 inhibitor 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 fumarate dihydrate.

38. The pharmaceutical composition of any one of claims 23-26, wherein the JAK2 inhibitor is (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile phosphoric acid salt.

39. The use of any one of claims 27-32, wherein the JAK2 inhibitor is (3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile phosphoric acid salt.

40. The use of any one of claims 27-32, wherein ALK2 inhibitor 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 fumarate dihydrate.