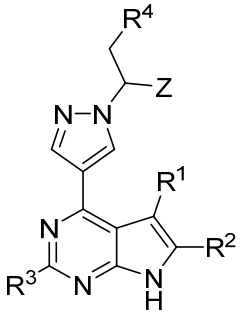
CLAIMS

1. A combination therapy comprising an ALK2 inhibitor, or pharmaceutically acceptable salt thereof, and a JAK2 inhibitor having the Formula I:



(**I**)

or a pharmaceutically acceptable salt thereof;

wherein

R^1, R^2 and R^3 are independently selected from the group consisting of hydrogen, halo, and C_{1-4} alkyl;

R^4 is selected from the group consisting of hydrogen, halo, cyano, nitro, hydroxy, C_{1-4} alkyl, and C_{1-4} alkoxy; and

Z is 3-6 membered cycloalkyl;

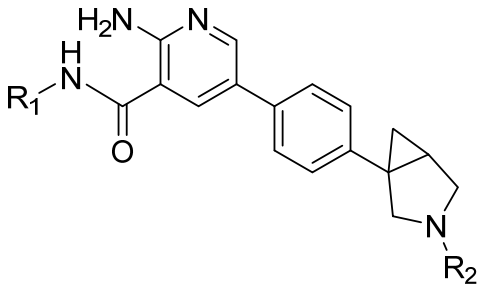
for use in the treatment of cancer in a subject in need thereof.

2. The combination therapy of claim 1, wherein R^1, R^2 and R^3 are all hydrogen, and R^4 is cyano.

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

4. The combination therapy of any one of claims 1-3, wherein the JAK2 inhibitor of Formula I 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.

5. The combination therapy of any one of claims 1-4, wherein the ALK2 inhibitor is a compound of Formula II:



(**II**)

or a pharmaceutically acceptable salt thereof;

wherein

R_1 is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C_1-C_3 alkoxy;

R^2 is selected from the group consisting of C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R^3; and

R^3 is selected from the group consisting of hydroxy, halo, cyano, nitro, SO_2-C_1-C_3 alkyl, and SO_3H.

6. The combination therapy of claim 5, wherein R_1 is bridged C_8-cycloalkyl substituted with hydroxy.

7. The combination therapy of claim 5 or 6, wherein R_2 is tetrahydropyran.

8. The combination therapy of any one of claims 1-7, wherein the ALK2 inhibitor of Formula II 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.

9. The combination therapy of claim 8, wherein the ALK2 inhibitor of Formula II 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. The combination therapy of claim 8, wherein the ALK2 inhibitor of Formula II 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.

11. The combination therapy of any one of claims 1-10, wherein the ALK2 inhibitor and JAK2 inhibitor are to be administered in a single formulation.

12. The combination therapy of claim 11, further comprising a pharmaceutically acceptable carrier.

13. The combination therapy of any one of claims 1-10, wherein the ALK2 inhibitor and JAK2 inhibitor are to be administered separately.

14. The combination therapy of any one of claims 1-13, wherein the cancer is a myeloproliferative neoplasm or a myelodysplastic syndrome.

15. The combination therapy of claim 14, 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).

16. The combination therapy of claim 14 or 15, wherein the cancer is myelofibrosis (MF).

17. The combination therapy of any one of claims 14-16, wherein the cancer is selected from the group consisting of primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis.

18. The combination therapy of any one of claims 1-17, wherein the subject is human.

19. The combination therapy of any one of claims 1-18, wherein the treatment comprises ~~administering~~ the ALK2 inhibitor and the JAK2 inhibitor to be administered at substantially the same time.

20. The combination therapy of any one of claims 1-10 and 13-18, wherein the treatment comprises ~~administering~~ the ALK2 inhibitor and the JAK2 inhibitor to be administered at different times.

21. The combination therapy of claim 20, wherein the ALK2 inhibitor is to be administered to the subject, followed by ~~administration of~~ the JAK2 inhibitor to be administered to the subject.

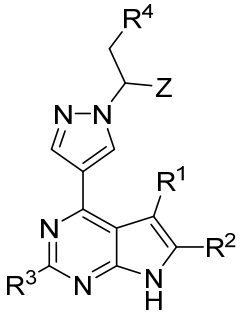
22. The combination therapy of claim 20, wherein the JAK2 inhibitor is to be administered to the subject, followed by ~~administration of~~ the ALK2 inhibitor to be administered to the subject.

23. The combination therapy of any one of claims 1-22, 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.

24. 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.

25. A pharmaceutical combination comprising

(i) a JAK2 inhibitor having the Formula I:



(**I**)

or a pharmaceutically acceptable salt thereof;

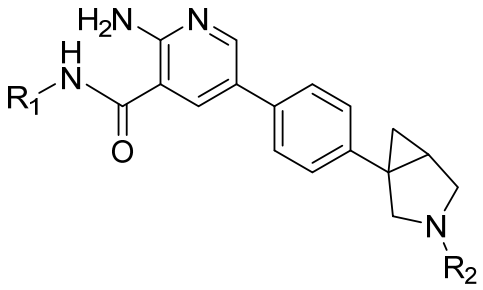
wherein

R^1, R^2 and R^3 are independently selected from the group consisting of hydrogen, halo, and C_{1-4} alkyl;

R^4 is selected from the group consisting of hydrogen, halo, cyano, nitro, hydroxy, C_{1-4} alkyl, and C_{1-4} alkoxy;

Z is 3-6 membered cycloalkyl; and

(ii) an ALK2 inhibitor having the Formula II:



(**II**)

or a pharmaceutically acceptable salt thereof;

wherein

R_1 is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C_1-C_3 alkoxy;

R^2 is selected from the group consisting of C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R^3; and

R^3 is selected from the group consisting of hydroxy, halo, cyano, nitro, SO_2-C_1-C_3 alkyl, and SO_3H.

26. The pharmaceutical combination of claim 25, 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.

27. The pharmaceutical combination of claim 25 or 26, 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.

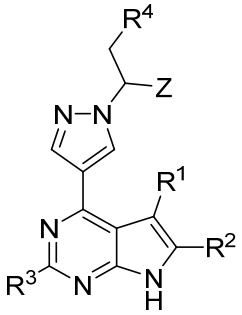
28. The pharmaceutical combination of any one of claims 25-27, wherein the ALK2 inhibitor is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-(3-(tetrahydro-2H-pyran-4-yl)-3-aza-bicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.

29. The pharmaceutical combination of any one of claims 25-28, 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.

30. The pharmaceutical combination of any one of claims 25-28, 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.

31. A pharmaceutical composition comprising an ALK2 inhibitor, a pharmaceutically acceptable carrier, and a JAK2 inhibitor having the Formula I:



(**I**)

or a pharmaceutically acceptable salt thereof;

wherein

R^1, R^2 and R^3 are independently selected from the group consisting of hydrogen, halo, and C_{1-4} alkyl;

R^4 is selected from the group consisting of hydrogen, halo, cyano, nitro, hydroxy, C_{1-4} alkyl, and C_{1-4} alkoxy; and

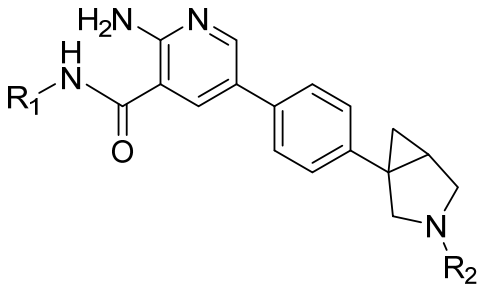
Z is 3-6 membered cycloalkyl.

32. The pharmaceutical composition of claim 31, wherein R^1, R^2 and R^3 are all hydrogen, and R^4 is cyano.

33. The pharmaceutical composition of claim 31 or 32, 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.

34. The pharmaceutical composition of any one of claims 31-33, 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.

35. The pharmaceutical composition of any one of claims 31-34, wherein the ALK2 inhibitor is a compound of Formula II:



(**II**)

or a pharmaceutically acceptable salt thereof;

wherein

R_1 is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C_1-C_3 alkoxy;

R^2 is selected from the group consisting of C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R^3; and

R^3 is selected from the group consisting of hydroxy, halo, cyano, nitro, SO_2-C_1-C_3 alkyl, and SO_3H.

36. The pharmaceutical composition of claim 35, wherein R_1 is bridged C_8-cycloalkyl substituted with hydroxyl.

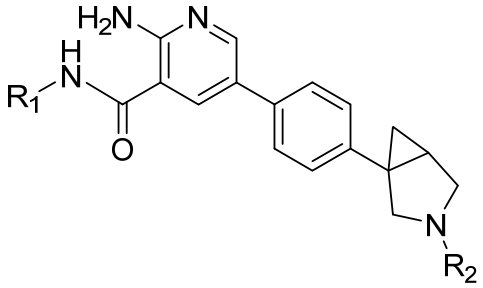
37. The pharmaceutical composition of claim 35 or 36, wherein R_2 is tetrahydropyran.

38. The pharmaceutical composition of any one of claims 31-37, wherein the ALK2 inhibitor is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-(3-(tetrahydro-2H-pyran-4-yl)-3-aza-bicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof.

39. The pharmaceutical composition of any one of claims 31-38, 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.

40. The pharmaceutical composition of any one of claims 31-38, 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.

41. ~~A method of treating myelofibrosis (MF) comprising administering to a subject in need thereof~~ Use of an ALK2 inhibitor that is a compound of Formula II:



(**II**)

or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of myelofibrosis (MF) in a subject;

wherein

R_1 is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C_1-C_3 alkoxy;

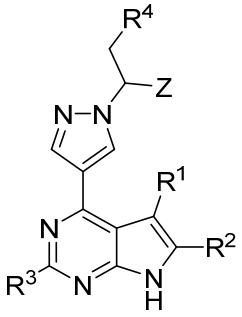
R^2 is selected from the group consisting of C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R^3; and

R^3 is selected from the group consisting of hydroxy, halo, cyano, nitro, SO_2-C_1-C_3 alkyl, and SO_3H;

wherein the compound of Formula II is to be administered as a monotherapy.

42. The ~~method~~ use of claim 41, wherein the compound of Formula II is 2-amino-N-(4-hydroxy-bicyclo-[2.2.2]octan-1-yl)-5-(4-(3-(tetrahydro-2H-pyran-4-yl)-3-aza-bicyclo[3.1.0]-hexan-1-yl)phenyl)nicotinamide, or a pharmaceutically acceptable salt thereof, wherein the compound of Formula II is administered as a monotherapy.

43. ~~A method of treating myelofibrosis (MF) induced anemia comprising administering to a subject in need thereof~~ Use of a JAK2 inhibitor having the Formula I:



(**I**)

or a pharmaceutically acceptable salt thereof;

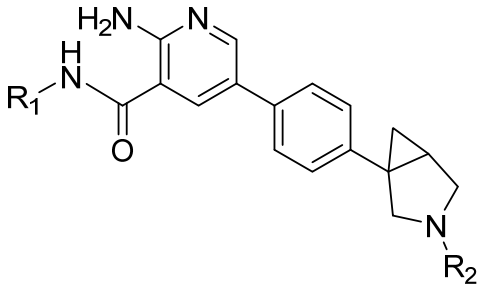
wherein

R^1, R^2 and R^3 are independently selected from the group consisting of hydrogen, halo, and C_{1-4} alkyl;

R^4 is selected from the group consisting of hydrogen, halo, cyano, nitro, hydroxy, C_{1-4} alkyl, and C_{1-4} alkoxy; and

Z is 3-6 membered cycloalkyl;

and an ALK2 inhibitor that is a compound of Formula II:



(**II**)

or a pharmaceutically acceptable salt thereof;

wherein

R_1 is bridged 5-10 membered cycloalkyl optionally substituted one, two, or three times with hydroxyl or C_1-C_3 alkoxy;

R^2 is selected from the group consisting of C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, 3-6 membered cycloalkyl, and 3-6 membered heterocycloalkyl, all of which are optionally substituted with R^3; and

R^3 is selected from the group consisting of hydroxy, halo, cyano, nitro, SO_2-C_1-C_3 alkyl, and SO_3H,

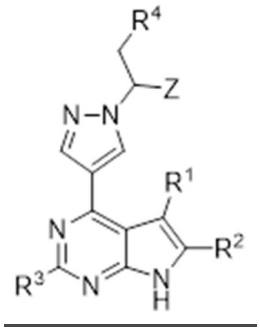
in the preparation of a medicament for the treatment of myelofibrosis (MF)-induced anemia in a subject.

44. The ~~method~~ use of claim 43, wherein

the JAK2 inhibitor of Formula I 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 of Formula II 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.

45. Use of an ALK2 inhibitor, or pharmaceutically acceptable salt thereof, and a JAK2 inhibitor having the Formula I:



(I)

or a pharmaceutically acceptable salt thereof; in the preparation of a medicament for a combination therapy in the treatment of cancer in a subject;

wherein

R1, R2 and R3 are independently selected from the group consisting of hydrogen, halo, and C1-4 alkyl;

R4 is selected from the group consisting of hydrogen, halo, cyano, nitro, hydroxy, C1-4 alkyl, and C1-4 alkoxy; and

Z is 3-6 membered cycloalkyl.

46. The use of claim 45, wherein the cancer is a myeloproliferative neoplasm or a myelodysplastic syndrome.

47. The use of claim 45, 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).

48. 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.