WHAT IS CLAIMED:

~~1. A method for treating anemia in a subject in need thereof, comprising:~~

~~administering to a subject~~Use of an activin receptor type IIB (ActRIIB) ligand trap~~;~~ and

1. ~~administering to~~ fedratinib in the ~~subject~~manufacture of a medicament for treating anemia in a subject in need thereof, wherein the ActRIIB ligand trap and fedratinib or a pharmaceutically acceptable salt and/or hydrate thereof are to be administered to the subject.

~~A method~~

2. Use of an activin receptor type IIB (ActRIIB) ligand trap and fedratinib in the manufacture of a medicament for treating anemia in a subject in need thereof, ~~comprising~~wherein:

(a)~~ taking~~ a first measurement of hemoglobin (Hgb) level is to be taken in a subject;

(b) ~~administering to the subject~~ an initial dose of an ActRIIB ligand trap is to be administered to the subject;

~~(c) administering to the subject~~(c) fedratinib or a pharmaceutically acceptable salt and/or hydrate thereof is to be administered;

(d)~~ taking~~ a second measurement of hemoglobin (Hgb) level is to be taken in the subject at the end of a first period of time after the administration of the initial dose of an ActRIIB ligand trap; and

~~(e) administering to the subject~~(e) a subsequent dose of the ActRIIB ligand trap is to be administered based on the second measurement of hemoglobin (Hgb) level as compared to the first measurement of hemoglobin (Hgb) level, or based on number of red blood cell transfusion that the subject received during the first period of time.

3. The ~~method~~use of claim 1 or 2, wherein the ActRIIB ligand trap and fedratinib or pharmaceutically acceptable salt or hydrate thereof are to be concomitantly administered.

~~4. The method~~use of any one of claims 1 to ~~3, wherein the co-administration of the ActRIIB ligand trap and fedratinib or pharmaceutically acceptable salt or hydrate thereof is pharmaceutically effective to treat anemia.~~

5.4. The method of any one of claims 1 to 4,3, wherein the subject is a subject is diagnosed with myelofibrosis.

6. The methoduse of claim 5,4, wherein the myelofibrosis is a myeloproliferative neoplasms (MPN)-associated myelofibrosis.

7.5. The method of claim 5, or wherein the myelofibrosis is intermediate or High-Risk Primary Myelofibrosis (PMF), Post-Polycythemia Vera Myelofibrosis (post-PV MF), or Post-Essential Thrombocythemia Myelofibrosis (post-ET MF).

8. The method of claim 7, wherein the myelofibrosis is intermediate or high-risk primary myelofibrosis (PMF).

9. The method of claim 7, wherein the myelofibrosis is intermediate or high-risk post-polycythemia vera myelofibrosis (post-PV MF).

10. The method of claim 7, wherein the myelofibrosis is intermediate or high-risk post-essential thrombocythemia myelofibrosis (post-ET MF).

11.6. The methoduse of any one of claims 1 to 10,5, wherein the subject is a human.

12. The methoduse of any one of claims 1 to 11, wherein the anemia is associated with myeloproliferative neoplasms (MPN)-associated myelofibrosis.

13. The method of any one of claims 1 to 11,6, wherein the subject is red blood cell (RBC) transfusion dependent or non-transfusion dependent.

14. The method of any one of claims 1 to 13, wherein the subject is RBC transfusion dependent.

15.7. The method of claim 14,optionally wherein the subject has received 4 to 12 RBC units in RBC transfusion within 84 days prior to administering of the ActRIIB ligand trap.

16.8. The methoduse of claim 1, wherein the subject has a hemoglobin (Hgb) level of less than 11.5 g/dL without red blood cell (RBC) transfusion.

~~17.~~ The ~~method~~use of any one of claims 1 to ~~13,~~6, wherein the subject is non-transfusion dependent~~.~~

~~18.~~9. ~~The method of claim 17,~~ optionally wherein the subject has received less than 4 red blood cell (RBC) units in RBC transfusion within 84 days prior to administering of the ActRIIB ligand trap.

~~19.~~10. The ~~method~~use of claim ~~17,~~9, wherein the subject has a hemoglobin (Hgb) level of less than 9.5 g/dL.

~~20.~~11. The ~~method~~use of any one of claims 1 to ~~19,~~10, wherein the subject has been treated with fedratinib for at least 8 weeks, at least 16 weeks, at least 24 weeks, at least 32 weeks, or at least 40 weeks prior to administration of the initial dose of the ActRIIB ligand trap and concomitantly administration of fedratinib or pharmaceutically acceptable salt or hydrate thereof.

~~21.~~12. The ~~method~~use of any one of claims 1 to ~~20,~~11, wherein the subject has been previously treated with ruxolitinib.

~~22.~~13. The ~~method~~use of any one of claims 1 to ~~21,~~12, wherein the fedratinib or pharmaceutically acceptable salt or hydrate thereof is to be administered daily.

~~23.~~ The ~~method~~use of any one of claims 1 to ~~22,~~13, wherein the fedratinib or pharmaceutically acceptable salt or hydrate thereof is to be administered orally~~.~~

~~24.~~14. ~~The method of any one of claims 1 to 23, wherein the fedratinib or pharmaceutically acceptable salt or hydrate thereof is administered~~, optionally at a dosage of 400 mg/day.

~~25.~~15. The ~~method~~use of any one of claims 1 to ~~24,~~14, wherein the ActRIIB ligand trap is to be administered once at the beginning of every treatment cycle, wherein each cycle is 21 days.

~~26.~~16. The ~~method~~use of any one of claims 1 to ~~25,~~15, wherein the ActRIIB ligand trap is to be administered to the subject for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 cycles.

~~27.~~17. The ~~method~~use of any one of claims 1 to ~~26,~~16, wherein the ActRIIB ligand trap is to be administered to the subject subcutaneously.

~~28.~~ The ~~method~~use of any one of claims 1 to ~~27,~~17, wherein the ~~pharmaceutically effective amount~~initial dose of the ActRIIB ligand trap to be administered is 0.6 mg/kg, 0.8 mg/kg, 1 mg/kg, 1.33 mg/kg, or 1.75 mg/kg~~.~~

~~29.~~18. ~~The method of claim 28, wherein the pharmaceutically effective amount of the ActRIIB ligand trap administered is~~, preferably 1.33 mg/kg.

~~30.~~ The ~~method~~use of any one of claims 2 to ~~27,~~17, wherein the first measurement of hemoglobin (Hgb) level is taken prior to ~~the administration of the initial dose of the ActRIIB ligand trap.~~

~~31.~~19. ~~The method of any one of claims 2 to 27, wherein the first measurement of hemoglobin (Hgb) level is taken~~or concurrently with the administration of the initial dose of the ActRIIB ligand trap~~, or taken about 3 weeks, 6 weeks, 9 weeks, 12 weeks, 15 weeks, 18 weeks, 21 weeks, or 24 weeks after the administration of the initial dose of the ActRIIB ligand trap.~~.

~~32.~~20. ~~The method of any one of claims 2 to 31,~~The use of claim 2, wherein the second measurement of hemoglobin (Hgb) level is taken about 3 weeks, 6 weeks, 9 weeks, 12 weeks, 15 weeks, 18 weeks, 21 weeks, 24 weeks, 7 months, 8 months, 9 months, 10 months, 11 months, or 12 months after the administration of the initial dose of the ActRIIB ligand trap~~ is administered to the subject~~.

~~33.~~21. The ~~method~~use of any one of claims 2 to ~~32,~~20, wherein the first period of time is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, or 8 weeks.

~~34.~~ The ~~method of any one of claims 33, wherein the first period of time is 6 weeks.~~

~~35.~~ The ~~method~~use of any one of claims 2 to ~~34, wherein the initial dose of the ActRIIB ligand trap is 1.33 mg/kg.~~

~~36. The method of any one of claims 2 to 35, wherein the subsequent dose of the ActRIIB ligand trap is 0.6 mg/kg, 0.8 mg/kg, 1.0 mg/kg, 1.33 mg/kg, or 1.75 mg/kg.~~

~~37. The method of any one of claims 2 to 35, wherein the subsequent dose of the ActRIIB ligand trap is 1.33 mg/kg.~~

~~38.~~22. ~~The method of any one of claims 2 to 35,~~21, wherein when the second measurement of Hgb level is 2 g/dL or more higher than the first measurement of Hgb level, the subsequent dose of the ActRIIB ligand trap is lower than the initial dose of the ActRIIB ligand trap.

~~39.~~23. The ~~method~~use of any one of claims 2 to ~~35,~~21, wherein when the subject has one or more RBC transfusion during the first period of time, or the second measurement of Hgb level is between 0 to about 1 g/dL higher than the first measurement of Hgb level, or the first measurement of Hgb level decreases 1 g/dL or more in a transfusion-free period of approximately 6 weeks, the subsequent dose of the ActRIIB ligand trap is higher than the initial dose of the ActRIIB ligand trap.

~~40.~~24. The ~~method~~use of any one of claims 2 to ~~35,~~21, wherein the subsequent dose of the ActRIIB ligand trap is the same as the initial dose of the ActRIIB ligand trap.

~~41. The method~~use of any one of claims ~~1 to 40, further comprising:~~

~~grading hematological, hepatic, non-hematological, or gastrointestinal event in the subject as Grade 1, 2, 3, 4, or 5 according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE); and~~

~~administering a subsequent dose of fedratinib or pharmaceutically acceptable salt or hydrate thereof.~~

~~42.~~25. ~~The method of claim 41,~~2-24, wherein the subsequent dose of fedratinib or pharmaceutically acceptable salt or hydrate thereof is 300 mg/day, 200 mg/day, or 100 mg/day.

~~43. The method~~use of any one of claims 1 to ~~42, wherein the ActRIIB ligand trap is a humanized fusion protein consisting of the extracellular domain of ActRIIB and the human IgG1 Fc domain.~~

~~44.~~26. ~~The method of any one of claims 1 to 42,~~25, wherein the ActRIIB ligand trap is a fusion-protein comprising the extracellular domain of ActRIIB and ~~the~~a human IgG1 Fc domain, optionally wherein the fusion-protein is a humanized fusion protein.

~~45.~~27. The ~~method~~use of any one of claims 1 to ~~42,~~25, wherein the ActRIIB ligand trap is a polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) 90% identical to SEQ ID NO:3;

(b) 95% identical to SEQ ID NO:3;

(c) 98% identical to SEQ ID NO:3;

(d) SEQ ID NO:4;

(e) 90% identical to SEQ ID NO:6;

(f) 95% identical to SEQ ID NO:6;

(g) 98% identical to SEQ ID NO:6;

(h) SEQ ID NO:7;

(i) 90% identical to SEQ ID NO:7;

(j) 95% identical to SEQ ID NO:7;

(k) 98% identical to SEQ ID NO:7;

(l) SEQ ID NO:8;

(m) 90% identical to SEQ ID NO:11;

(n) 95% identical to SEQ ID NO:11;

(o) 98% identical to SEQ ID NO:11; and

(p) SEQ ID NO:11~~.~~,

~~46. The method of any one of claims 1 to 42,~~preferably wherein the ActRIIB ligand trap is a polypeptide comprising ~~an~~the amino acid sequence ~~selected from the group consisting of:~~

~~(a)~~ ~~90% identical to~~ of SEQ ID NO:11~~; .~~.

~~(b) 95% identical to SEQ ID NO:11;~~

~~(c) 98% identical to SEQ ID NO:11; and~~

~~(d) SEQ ID NO:11.~~

~~47.~~ The ~~method~~use of any one of claims 1 to ~~42,~~25, wherein the ActRIIB ligand trap is a polypeptide ~~comprising the amino acid sequence of SEQ ID NO:11.~~

~~48.~~28. ~~The method of any one of claims 1 to 42, wherein the ActRIIB ligand trap is a polypeptide is~~ encoded by the nucleotide sequence of SEQ ID NO:34 or a degenerate version of SEQ ID NO:34.

~~49. The method of any one of claims 1 to 47, wherein the method increases the hemoglobin (Hgb) level in the subject by at least 0.5 g/dL, at least 1.0 g/dL, at least 1.5 g/dL, at least 2.0 g/dL, or at least 2.5 g/dL.~~

~~50. The method of claim 49, wherein the method increases the hemoglobin (Hgb) level in the subject by at least 1.5 g/dL.~~

~~51. The method of any one of claims 1 to 47, wherein the method reduces at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 units of red blood cell (RBC) transfusions received by the subject within a period of 56 days.~~

~~52. The method of claim 51, wherein the method reduces at least 4 units of RBC transfusions received by the subject within a period of 56 days.~~

~~53. The method of any one of claims 1 to 47, wherein the method reduces at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, or at least 10 units of red blood cell (RBC) transfusions received by the subject within a period of 84 days.~~

~~54. The method of any one of claims 1 to 47, wherein the method increases the hemoglobin (Hgb) level in the subject by at least 1.5 g/dL over a consecutive 84 day period.~~

~~55. The method of any one of claims 1 to 47, wherein the subject becomes red blood cell (RBC) transfusion free over a consecutive period of 84 days.~~

~~56. The method of any one of claims 1 to 55, wherein the method increases hemoglobin (HGB) levels in the subject to levels equal to or about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 100%, 200%, or 500% greater than HGB levels in the subject prior to said treating.~~

~~57. The method of any one of claims 1 to 56, wherein the method increases hematocrit (HCT) levels in the subject to levels equal to or about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 100%, 200%, or 500% greater than HCT levels in the subject prior to said treating.~~

~~58. The method of any one of claims 1 to 57, wherein the method reduces mean corpuscular volume (MCV) levels in the subject to levels equal to or about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, or 100%, less than MCV levels in the subject prior to said treating.~~

~~59. The method of any one of claims 1 to 58, wherein the method increases cellular hemoglobin concentration (CHC) levels in the subject to levels equal to or about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 100%, 200%, or 500% greater than CHC levels in the subject prior to said treating~~

~~60. The method of any one of claims 1 to 59, wherein the method reduces red blood cell distribution width (RDW) levels in the subject to levels equal to or about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, or 100%, less than the RDW levels in the subject prior to said treating~~

~~61. The method of any one of claims 1 to 60, wherein the levels of reticulocytes in the subject remain in the range equal to or about 0.1%, 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, or 20% above or below the levels of reticulocytes in the subject prior to said treating.~~

~~62. The method of any one of claims 1 to 61, wherein the levels of reticulocytes in the subject remain in the range equal to or about 0.1%, 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, or 20% above or below the levels of reticulocytes in a reference population.~~

~~The method of any one of claims 1 to 62, wherein the levels of white blood cells in the subject remain in the range equal to or about 0.1%, 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, or 20% above or below the levels of white blood cells in the subject prior to said treating.~~