WHAT IS CLAIMED:

1. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising:~~wherein the ActRIIB ligand trap is to be administered to the subject; and the mTOR inhibitor is to be administered to the subject.

~~administering to the subject an ActRIIB ligand trap; and~~

~~administering to the subject an mTOR inhibitor.~~

2. The ~~method~~ use of claim 1, wherein the anemia is an anemia associated with ineffective erythropoiesis, thalassemia, alpha-thalassemia, beta-thalassemia, myelodysplastic syndromes (MDS), or non-proliferative chronic myelomonocytic leukemia (CMML).

3. The ~~method~~ use of claim 1 or 2, wherein the mTOR inhibitor is rapamycin.

4. The use~~method~~ of any of claims 1 to 3, wherein the mTOR inhibitor is a pharmaceutically acceptable salt or hydrate of rapamycin.

5. The use~~method~~ of any one of claims 1 to 4, wherein the ActRIIB ligand trap is a polypeptide comprising:

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

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

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

(d) SEQ ID NO:11.

6. The use~~method~~ of any one of claims 1 to 5, wherein the ActRIIB ligand trap is a polypeptide comprising an amino acid sequence of SEQ ID NO:11.

7. The use~~method~~ of any one of claims 1 to 6, wherein the ~~method~~ medicament is capable of increasing~~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.

8. The use~~method~~ of any one of claims 1 to 7, wherein the medicament is capable of increasing~~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.

9. The ~~method~~ use of any one of claims 1 to 8, wherein the medicament is capable of reducing~~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.

10. The ~~method~~ use of any one of claims 1 to 9, wherein the medicament is capable of increasing ~~method increases~~ corpuscular 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.

11. The ~~method~~ use of any one of claims 1 to 10, wherein the medicament is capable of reducing ~~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.

12. The ~~method~~ use of any one of claims 1 to 11, 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.

13. The ~~method~~ use of any one of claims 1 to 11, 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.

14. The ~~method~~ use of any one of claims 1 to 13, 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.

15. The ~~method~~ use of any one of claims 1 to 13, 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 a reference population.

16. The ~~method~~ use of any one of claims 1 to 15, wherein the mTOR inhibitor is to be administered before or concurrently with the administration of ActRIIB ligand trap.

17. The ~~method~~ use of any one of claims 1 to 15, wherein the subject has been previously treated with the mTOR inhibitor prior the administration of ActRIIB ligand trap.

18. The ~~method~~ use of any one of claims 1 to 15, wherein the subject has been previously treated with the ActRIIB ligand trap prior the administration of mTOR inhibitor.

19. The ~~method~~ use of any one of claims 1 to 18, wherein the subject is red blood cell non-transfusion-dependent.

20. The ~~method~~ use of any one of claims 1 to 18, wherein the subject is red blood cell transfusion-dependent.

21. The ~~method~~ use of any one of claims 1 to 20, wherein the ActRIIB ligand trap is to be administered with a dose of 0.6 mg/kg, 0.8 mg/kg, 1 mg/kg, 1.33 mg/kg, or 1.75 mg/kg.

22. The ~~method~~ use of any one of claims 1 to 20, wherein the ActRIIB ligand trap is to be administered to the subject once every 21 days.

23. The ~~method~~ use of any one of claims 1 to 22, wherein the ActRIIB ligand trap is to be administered to the subject subcutaneously.

24. The ~~method~~ use of any one of claims 1 to 23, wherein the subject is a human.

25. The ~~method~~ use of any one of claims 13, 15, and 16 to 24, wherein the reference population consists of 1, 5, 10, 25, 50, 75, 100, 200, 250, 300, 400, 500, or 1000 individuals.

26. The ~~method~~ use of any one of claims 13, 15, and 16 to 25, wherein the reference population consists of healthy individuals.

27. The ~~method~~ use of any one of claims 13, 15, and 16 to 26 wherein the reference population consists of people of the same age, weight, and/or gender as the subject.

28. The ~~method~~ use of any one of claims 1 to 27, wherein the mTOR inhibitor is to be administered orally.

29. The ~~method~~ use of any one of claims 1 to 28, wherein the mTOR inhibitor is to be administered at a dose of 0.1 mg/kg, 0.2 mg/kg, 0.5 mg/kg, 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg, 10 mg/kg, or 15 mg/kg.

30. The ~~method~~ use of any one of claims 1 to 29, wherein the mTOR inhibitor is to be administered daily.

31. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament ~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising~~wherein:

~~administering to the subject an~~ the ActRIIB ligand trap is to be administered to the subject; and

~~administering to the subject an~~ the mTOR inhibitor is to be administered to the subject,

wherein the ~~method~~ medicament is capable of increasing~~s~~ hemoglobin (HGB) levels in a reference population 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 who received either an ActRIIB ligand trap or an mTOR inhibitor, but not together.

32. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising~~wherein:

~~administering to the subject an~~the ActRIIB ligand trap is to be administered to the subject; and

~~administering to the subject an~~ the mTOR inhibitor is to be administered to the subject,

wherein the ~~method increases~~medicament is capable of increasing 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 HGB levels in a reference population who received either an ActRIIB ligand trap or an mTOR inhibitor, but not together.

33. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament ~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising~~wherein:

~~administering to the subject an~~the ActRIIB ligand trap is to be administered to the subject; and

~~administering to the subject an~~the mTOR inhibitor is to be administered to the subject,

wherein the ~~method reduces~~medicamentis is capable of reducing 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%, 100%, 200%, or 500% less than hemoglobin (HGB) levels in a reference population who received either an ActRIIB ligand trap or an mTOR inhibitor, but not together.

34. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament ~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising~~wherein:

~~administering to the subject an~~ the ActRIIB ligand trap is to be administered to the subject; and

~~administering to the subject an~~ the mTOR inhibitor is to be administered to the subject,

wherein the ~~method increases~~medicament is capable of increasing corpuscular 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 hemoglobin (HGB) levels in a reference population who received either an ActRIIB ligand trap or an mTOR inhibitor, but not together.

35. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament ~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising~~wherein:

~~administering to the subject an~~ the ActRIIB ligand trap is to be administered to the subject; and

~~administering to the subject an~~ the mTOR inhibitor is to be administered to the subject,

wherein the ~~method reduces~~medicament is capable of reducing 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%, 100%, 200%, or 500% less than hemoglobin (HGB) levels in a reference population who received either an ActRIIB ligand trap or an mTOR inhibitor, but not together.

36. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament ~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising~~wherein:

~~administering to the subject an~~ the ActRIIB ligand trap is to be administered to the subject; and

~~administering to the subject an~~ the mTOR inhibitor is to be administered to the subject,

wherein the levels of reticulocytes in the subject deviant from normal levels of reticulocytes equal to or about 0.1%, 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, or 20% less as compared to the levels of reticulocytes in a reference population who received either an ActRIIB ligand trap or an mTOR inhibitor, but not together.

37. Use of an ActRIIB ligand trap and an mTOR inhibitor in the manufacture of a medicament ~~A method~~ for treating anemia or for enhancing late stage erythropoiesis in a subject in need thereof, ~~comprising~~wherein:

~~administering to the subject an~~ the ActRIIB ligand trap is to be administered to the subject; and

~~administering to the subject an~~ the mTOR inhibitor is to be administered to the subject,

wherein the levels of white blood cells in the subject deviant from normal levels of reticulocytes equal to or about 0.1%, 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, or 20% less as compared to the levels of reticulocytes in a reference population who received either an ActRIIB ligand trap or an mTOR inhibitor, but not together.

38. The ~~method~~ use of any one of claims 31 to 37, wherein the subject is a human.

39. The ~~method~~ use of any one of claims 31 to 38, wherein the reference population consists of 1, 5, 10, 25, 50, 75, 100, 200, 250, 300, 400, 500, or 1000 individuals.

40. The ~~method~~ use of any one of claims 31 to 39 wherein the reference population consists of people of the same age, weight, and/or gender as the subject.

41. The ~~method~~ use of any one of claims 31 to 40, wherein the reference population consists of individuals with anemia.

42. The ~~method~~ use of any one of claims 31 to 41, wherein the anemia is an anemia associated with ineffective erythropoiesis, thalassemia, alpha-thalassemia, beta-thalassemia,

myelodysplastic syndromes (MDS), or non-proliferative chronic myelomonocytic leukemia (CMML).

43. The ~~method~~ use of any one of claims 31 to 42, wherein the mTOR inhibitor is rapamycin.

44. The ~~method~~ use of any one of claims 31 to 43, wherein the mTOR inhibitor is a pharmaceutically acceptable salt or hydrate of rapamycin.

45. The ~~method~~ use of any one of claims 31 to 44, wherein the ActRIIB ligand trap is a polypeptide comprising:

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

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

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

(d) SEQ ID NO:11.

46. The ~~method~~ use of any one of claims 31 to 45, wherein the ActRIIB ligand trap is a polypeptide comprising an amino acid sequence of SEQ ID NO:11.

47. The ~~method~~ use of any one of claims 31 to 46, wherein the subject is red blood cell non-transfusion-dependent.

48. The ~~method~~ use of any one of claims 31 to 46, wherein the subject is red blood cell transfusion-dependent.

49. The ~~method~~ use of any one of claims 31 to 48, wherein the ActRIIB ligand trap is to be administered with a dose of 0.6 mg/kg, 0.8 mg/kg, 1 mg/kg, 1.33 mg/kg, or 1.75 mg/kg.

50. The use~~method~~ of any one of claims 31 to 49, wherein the ActRIIB ligand trap is to be administered to the subject once every 21 days.

51. The ~~method~~ use of any one of claims 31 to 50, wherein the ActRIIB ligand trap is to be administered to the subject subcutaneously.

52. The ~~method~~ use of any one of claims 31 to 51, wherein the mTOR inhibitor is to be administered orally.

53. The ~~method~~ use of any one of claims 31 to 52, wherein the mTOR inhibitor is to be administered at a dose of 0.1 mg/kg, 0.2 mg/kg, 0.5 mg/kg, 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg, 10 mg/kg, or 15 mg/kg.

54. The ~~method~~ use of any one of claims 31 to 53, wherein the mTOR inhibitor is to be administered daily.