There remains a need to provide alternative BMP-6 antibodies. In particular, there remains a need to provide potent BMP-6 antibodies that are selective for BMP-6 over other BMP family members, including BMP-7. There also remains a need to provide potent BMP-6 antibodies that are selective for BMP-6 over other BMP family members, including BMP-7, and produce a prolonged pharmacodynamic response. There also remains a need to provide potent BMP-6 antibodies that are selective for BMP-6 over other BMP family members, including BMP-7, for the treatment of ACD.

SUMMARY

In an aspect, there is provided an antibody, or antigen-binding fragment thereof, that binds to human BMP-6 (SEQ ID NO: 1), comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RSSENIYRNLA (SEQ ID NO: 2), the LCDR2 is the polypeptide of AATNLAD (SEQ ID NO: 3), the LCDR3 is the polypeptide of QGIWGTPLT (SEQ ID NO: 4), the HCDR1 is the polypeptide of GYTFTSYAMH (SEQ ID NO: 5), the HCDR2 is the polypeptide of YINPYNDGTKYNENFKG (SEQ ID NO: 6) or YINPYNRGTKYNENFKG (SEQ ID NO: 7), and the HCDR3 is the polypeptide of RPFGNAMDI (SEQ ID NO: 8).

In another aspect, there is provided a pharmaceutical composition comprising an antibody, or antigen-binding fragment thereof, as defined above, and an acceptable carrier, diluent, or excipient.

In a further aspect, there is provided a use of an antibody, or antigen-binding fragment thereof, as defined above, in the manufacture of a medicament for treating anemia

In yet another aspect, there is a method of increasing serum iron levels, reticulocyte count, red blood cell count, hemoglobin, and/or hematocrit, comprising administering an effective amount of the antibody, or antigen-binding fragment thereof, as defined above.

DETAILED DESCRIPTION OF EMBODIMENTS

Accordingly, the present invention provides an antibody, or antigen-binding fragment thereof, that binds to human BMP-6 (SEQ ID NO: 1), comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RSSENIYRNLA (SEQ ID NO: 2), the LCDR2 is the polypeptide of AATNLAD (SEQ ID NO: 3), the LCDR3 is the polypeptide of QGIWGTPLT (SEQ ID NO: 4), the HCDR1 is the polypeptide of GYTFTSYAMH (SEQ ID NO: 5), the HCDR2 is the polypeptide of YINPYNDGTKYNENFKG (SEQ ID NO: 6) or YINPYNRGTKYNENFKG (SEQ ID NO: 7), and the HCDR3 is the polypeptide of RPFGNAMDI (SEQ ID NO: 8).

In an embodiment, the present invention provides an antibody, or antigen-binding fragment thereof, that binds to human BMP-6 (SEQ ID NO: 1), comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RSSENIYRNLA (SEQ ID NO: 2), the LCDR2 is the polypeptide of AATNLAD (SEQ ID NO: 3), the LCDR3 is the polypeptide of QGIWGTPLT (SEQ ID NO: 4), the HCDR1 is the polypeptide of GYTFTSYAMH (SEQ ID NO: 5), the HCDR2 is the polypeptide of YINPYNDGTKYNENFKG (SEQ ID NO: 6), and the HCDR3 is the polypeptide of RPFGNAMDI (SEQ ID NO: 8).

In an embodiment, the present invention provides an antibody, or antigen-binding fragment thereof, that binds to human BMP-6 (SEQ ID NO: 1), comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR

of SEQ ID NO: 9, and the HCVR is the polypeptide of SEQ ID NO: 10 or SEQ ID NO: 11.

5. The antibody, or antigen-binding fragment thereof, of Claim 4, wherein the LCVR is the polypeptide of SEQ ID NO: 9, and the HCVR is the polypeptide of SEQ ID NO: 10.

6. The antibody, or antigen-binding fragment thereof, of Claim 4, wherein the LCVR is the polypeptide of SEQ ID NO: 9, and the HCVR is the polypeptide of SEQ ID NO: 11.

7. The antibody of Claim 1 or 4, comprising a light chain (LC) and a heavy chain (HC), wherein the LC is the polypeptide of SEQ ID NO: 12, and the HC is the polypeptide of SEQ ID NO: 13 or SEQ ID NO: 14.

8. The antibody of Claim 7, wherein the LC is the polypeptide of SEQ ID NO: 12, and the HC is the polypeptide of SEQ ID NO: 13.

9. The antibody of Claim 7, wherein the LC is the polypeptide of SEQ ID NO: 12, and the HC is the polypeptide of SEQ ID NO: 14.

10. The antibody of any one of Claim 1, 4, or 7, comprising two light chains and two heavy chains, wherein each light chain is the polypeptide of SEQ ID NO: 12, and each heavy chain is the polypeptide of SEQ ID NO: 13.

11. The antibody of any one of Claim 1, 4, or 7, comprising two light chains and two heavy chains, wherein each light chain is the polypeptide of SEQ ID NO: 12, and each heavy chain is the polypeptide of SEQ ID NO: 14.

12. A pharmaceutical composition comprising an antibody, or antigen-binding fragment thereof, of any one of Claims 1-11, and an acceptable carrier, diluent, or excipient.

13. ~~A method of treating anemia, comprising administering to a patient in need thereof, an effective amount of the~~Use of an antibody, or antigen-binding fragment thereof, of any one of Claims 1-11, in the manufacture of a medicament for treating anemia.

14. The ~~method~~ use according to Claim 13, wherein the anemia is anemia of chronic disease.

15. The ~~method~~ use according to Claim 14, wherein the anemia of chronic disease is selected from the group consisting of anemia of cancer, and anemia of chronic kidney disease.

16. A method of increasing serum iron levels, reticulocyte count, red blood cell count, hemoglobin, and/or hematocrit, comprising administering an effective amount of the antibody, or antigen-binding fragment thereof, of any one of Claims 1-11.

17. The antibody, or antigen-binding fragment thereof, of any one of Claims 1-11, for use in therapy.

18. The antibody, or antigen-binding fragment thereof, of any one of Claims 1-11, for use in the treatment of anemia.

19. The antibody, or antigen-binding fragment thereof, of Claim 18, wherein the anemia is anemia of chronic disease.

20. The antibody, or antigen-binding fragment thereof, of Claim 19, wherein the anemia of chronic disease is selected from the group consisting of anemia of cancer, and anemia of chronic kidney disease.