CLAIMS

What is claimed is:

1. A method for treating osteogenesis imperfecta (OI) in a subject in need thereof comprising administering to the subject a therapeutically effective amount of an antibody or an antigen binding fragment thereof that specifically binds to transforming growth factor beta (TGFβ).

2. The method of claim 1, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising three complementarity determining regions (CDRs) having amino acid sequences selected from the group consisting of SEQ ID NOs: 4, 5, and 6; and a light chain variable region comprising three CDRs having amino acid sequences selected from the group consisting of SEQ ID NOs: 7, 8, and 9.

3. The method of claim 1 or 2, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 10, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 11.

4. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof further comprises a human IgG4 constant region.

5. The method of claim 4, wherein the human IgG4 constant region comprises the amino acid sequence of SEQ ID NO: 12.

6. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof further comprises a human κ light chain constant region.

7. The method of claim 6, wherein the human κ light chain constant region comprises the amino acid sequence of SEQ ID NO: 13.

8. The method of any one of claims 1-3, wherein the antibody or antigen binding fragment thereof further comprises a human IgG4 constant region, and a human κ light chain constant region.

9. The method of claim 8, wherein the human IgG4 constant region comprises the amino acid sequence of SEQ ID NO: 12, and the human κ light chain constant region comprises the amino acid sequence of SEQ ID NO: 13.

10. The method of any one of the previous claims, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 14.

11. The method of any one of the previous claims, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 15.

12. The method of any one of the previous claims, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 14, and a light chain comprising the amino acid sequence of SEQ ID NO: 15.

13. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof binds to human TGFβ1, TGFβ2, and TGFβ3.

14. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof neutralizes human TGFβ1, TGFβ2, and TGFβ3.

15. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof improves a bone parameter selected from the group consisting of bone volume density (BV/TV), total bone surface (BS), bone surface density (BS/BV), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular spacing (Tb.Sp), and total volume (Dens TV).

16. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof inhibits bone resorption.

17. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof reduces a serum biomarker of bone resorption selected from the group consisting of urinary hydroxyproline, urinary total pyridinoline (PYD), urinary free deoxypyridinoline (DPD), urinary collagen type-I cross-linked N-telopeptide (NTX), urinary

or serum collagen type-I cross-linked C-telopeptide (CTX), bone sialoprotein (BSP), osteopontin (OPN), and tartrate-resistant acid phosphatase 5b (TRAP).

18. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof increases a serum biomarker of bone deposition selected from the group consisting of as total alkaline phosphatase, bone-specific alkaline phosphatase, osteocalcin, and type-I procollagen (C-terminal/N-terminal).

19. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof inhibits bone resorption.

20. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof promotes bone deposition.

21. The method of any one of the previous claims, wherein the antibody or antigen binding fragment thereof improves the function of a non-skeletal organ affected by OI selected from the group consisting of hearing function, lung function, and kidney function.

22. A method for treating osteogenesis imperfecta (OI) in a subject in need thereof comprising administering to the subject a therapeutically effective amount of an antibody or an antigen binding fragment thereof that binds to transforming growth factor beta (TGFβ), wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 14, and a light chain comprising the amino acid sequence of SEQ ID NO: 15.

23. A method for treating osteogenesis imperfecta (OI) in a subject in need thereof comprising administering to the subject a therapeutically effective amount of an antibody or an antigen binding fragment thereof that binds to transforming growth factor beta (TGFβ) in combination with at least one therapeutic agent.

24. The method of claim 23, wherein the agent is a bisphosphonate.

CLAIMS

What is claimed is:

1. Use of an antibody or an antigen binding fragment thereof that specifically binds to transforming growth factor beta (TGFβ) in the manufacture of a medicament for treating osteogenesis imperfecta (OI) in a subject in need thereof.

2. The use of an antibody or an antigen binding fragment thereof according to claim 1, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising three complementarity determining regions (CDRs) having amino acid sequences selected from the group consisting of SEQ ID NOs: 4, 5, and 6; and a light chain variable region comprising three CDRs having amino acid sequences selected from the group consisting of SEQ ID NOs: 7, 8, and 9.

3. The use of an antibody or an antigen binding fragment thereof according to claim 1 or 2, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 10, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 11.

4. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof further comprises a human IgG4 constant region.

5. The use of an antibody or an antigen binding fragment thereof according to claim 4, wherein the human IgG4 constant region comprises the amino acid sequence of SEQ ID NO: 12.

6. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof further comprises a human κ light chain constant region.

7. The use of an antibody or an antigen binding fragment thereof according to claim 6, wherein the human κ light chain constant region comprises the amino acid sequence of SEQ ID NO: 13.

8. The use of an antibody or an antigen binding fragment thereof according to any one of claims 1-3, wherein the antibody or antigen binding fragment thereof further comprises a human IgG4 constant region, and a human κ light chain constant region.

9. The use of an antibody or an antigen binding fragment thereof according to claim 8, wherein the human IgG4 constant region comprises the amino acid sequence of SEQ ID NO: 12, and the human κ light chain constant region comprises the amino acid sequence of SEQ ID NO: 13.

10. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 14.

11. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 15.

12. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 14 and a light chain comprising the amino acid sequence of SEQ ID NO: 15.

13. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof binds to human TGFβ1, TGFβ2, and TGFβ3.

14. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof neutralizes human TGFβ1, TGFβ2, and TGFβ3.

15. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof improves a bone parameter selected from the group consisting of bone volume density (BV/TV), total bone surface (BS), bone surface density (BS/BV), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular spacing (Tb.Sp), and total volume (Dens TV).

16. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof inhibits bone resorption.

17. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof reduces a serum biomarker of bone resorption selected from the group consisting of urinary hydroxyproline, urinary total pyridinoline (PYD), urinary free deoxypyridinoline (DPD), urinary collagen type-I cross-linked N-telopeptide (NTX), urinary or serum collagen type-I cross-linked C-telopeptide (CTX), bone sialoprotein (BSP), osteopontin (OPN), and tartrate-resistant acid phosphatase 5b (TRAP).

18. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof increases a serum biomarker of bone deposition selected from the group consisting of as total alkaline phosphatase, bone-specific alkaline phosphatase, osteocalcin, and type-I procollagen (C-terminal/N-terminal).

19. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof promotes bone deposition.

20. The use of an antibody or an antigen binding fragment thereof according to any one of the previous claims, wherein the antibody or antigen binding fragment thereof improves the function of a non-skeletal organ affected by OI selected from the group consisting of hearing function, lung function, and kidney function.

21. The use of an antibody or an antigen binding fragment thereof according to claim 1, in combination with at least one therapeutic agent.

22. The use of an antibody or an antigen binding fragment thereof according to claim 21, wherein the agent is selected from the group consisting of: a bisphosphonate, parathyroid hormone or a parathyroid hormone analog, calcitonin, and a selective estrogen receptor modulator (SERM).

23. The use of an antibody or an antigen binding fragment thereof according to claim 22, wherein the agent is parathyroid hormone or a parathyroid hormone analog.

24. The use of an antibody or an antigen binding fragment thereof according to claim 23, wherein the subject has type I OI.