

CLAIMS

1. Use of an anti-TGF β antibody or an antigen-binding fragment thereof in the manufacture of a medicament for use in treating moderate-to-severe osteogenesis imperfecta (OI) in a human subject in need thereof, wherein a therapeutically effective amount of an anti-TGF β antibody or an antigen-binding fragment thereof is to be administered as a single dose to the subject, wherein the antibody or antigen-binding fragment comprises

heavy chain complementarity-determining regions (CDRs) 1-3 comprising SEQ ID NOs:4-6, respectively, and

light chain CDR1-3 comprising SEQ ID NOs:7-9, respectively,
wherein the therapeutically effective amount is 1-10 mg/kg.

2. The use of claim 1, wherein the antibody or antigen-binding fragment comprises a heavy chain variable domain comprising SEQ ID NO:10 and a light chain variable domain comprising SEQ ID NO:11.

3. The use of claim 1 or 2, wherein the antibody comprises a human IgG₄ constant region and/or a human κ light chain constant region.

4. The use of claim 3, wherein the human IgG₄ constant region comprises a S228P mutation (Eu numbering).

5. The use of claim 3, wherein the antibody comprises a heavy chain comprising SEQ ID NO:1 and a light chain comprising SEQ ID NO:2.
6. The use of claim 3, wherein the antibody comprises a heavy chain comprising SEQ ID NO:3 and a light chain comprising SEQ ID NO:2.
7. The use of any one of the preceding claims, wherein the antibody comprises a bone-targeting moiety, optionally wherein the bone-targeting moiety is a poly-aspartate peptide.
8. The use of claim 7, wherein the antibody comprises one or more poly-aspartate peptides.
9. The use of claim 8, wherein the antibody is fused to a poly-aspartate peptide at the N-terminus, or the C-terminus, or both termini, of the heavy chain, and/or at the C-terminus of the light chain, of the antibody or antigen-binding fragment.
10. The use of any one of claims 7-9, wherein the poly-aspartate peptide is D10 (SEQ ID NO:14).
11. The use of any one of the preceding claims, wherein the OI is type IV OI.
12. The use of any one of the preceding claims, wherein the human subject is an adult patient (≥ 18 years of age), or a pediatric patient (< 18 years of age).

13. The use of any one of the preceding claims, wherein the human subject has a mutation in a *COL1A1* or *COL1A2* gene, optionally wherein the mutation is a glycine substitution mutation in the *COL1A1* or *COL1A2* gene or a valine deletion in the *COL1A2* gene.
14. The use of any one of the preceding claims, wherein the administration improves a bone parameter selected from the group consisting of bone mineral density (BMD), 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).
15. The use of claim 14, wherein the bone parameter is lumbar spine areal BMD (LS aBMD), optionally wherein the LS aBMD increases by at least 1-10% after the administration relative to baseline level.
16. The use of any one of the preceding claims, wherein the administration decreases bone turnover and/or osteocyte density, optionally wherein the decreased bone turnover is indicated by a decrease in serum CTX or an increase in serum osteocalcin (OCN).
17. The use of any one of claims 1-16, wherein the therapeutically effective amount is 1 mg/kg.
18. The use of any one of claims 1-16, wherein the therapeutically effective amount is 4 mg/kg.

19. The use of any one of the preceding claims, wherein the administration is repeated every month, every two months, every three months, every six months, every nine months, or every twelve months.
20. The use of any one of the preceding claims, wherein the antibody or antigen-binding fragment is to be administered by intravenous infusion.
21. The use of any one of the preceding claims, wherein a bisphosphonate, parathyroid hormone, calcitonin, teriparatide, or an anti-sclerostin agent is also to be administered to the subject.
22. The use of claim 21, wherein the bisphosphonate is selected from alendronate, pamidronate, zoledronate, and risedronate.