CLAIMS

What is claimed is:

1. A monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) and neutralizes at least one activity of NOTUM.

2. The antibody of claim 1, wherein the antibody binds to a NOTUM selected from mouse NOTUM, guinea pig NOTUM, cynomolgus monkey NOTUM, and rhesus monkey NOTUM.

3. The antibody of any one of the preceding claims, wherein the antibody reduces NOTUM activity in a trisodium 8-octanoyloxypyrene-1,3,6-trisulfonate (OPTS) assay *in vitro*, and/or reduces NOTUM activity in a Wnt signaling assay *in vitro*.

4. The antibody of any one of the preceding claims, wherein upon administration to a subject the antibody increases serum PINP levels *in vivo*, increases bone mineral density *in vivo*, increases midshaft femur cortical thickness *in vivo*, increases midshaft femur bone area *in vivo*, increases midshaft humerus cortical thickness *in vivo*, increases endocortical bone formation *in vivo*, increases the proportion of cortical bone volume in the LV5 vertebral body *in vivo*, and/or increases the proportion of femoral neck bone volume to femoral neck total volume *in vivo*.

5. The antibody of any one of the preceding claims, wherein the antibody binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with K_D of less than 50 nM.

6. The antibody of claim 5, wherein the K_D is less than 20 nM.

7. The antibody of claim 6, wherein the K_D is less than 10 nM.

8. The antibody of any one of the preceding claims, wherein the antibody has at least one binding characteristic selected from:

a) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 83 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 84;

b) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 85 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 86;

c) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 94;

d) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 99;

e) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 95 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 2;

f) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO: 8;

g) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 15 and a light chain variable region having the amino acid sequence of SEQ ID NO: 16;

h) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 23 and a light chain variable region having the amino acid sequence of SEQ ID NO: 24;

i) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 31 and a light chain variable region having the amino acid sequence of SEQ ID NO: 32;

j) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 39 and a light chain variable region having the amino acid sequence of SEQ ID NO: 40;

k) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 47 and a light chain variable region having the amino acid sequence of SEQ ID NO: 48; and

l) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 55 and a light chain variable region having the amino acid sequence of SEQ ID NO: 56.

9. The antibody of any one of the preceding claims, wherein the antibody is selected from a mouse antibody, a chimeric antibody, a humanized antibody, and a human antibody.

10. The antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain and a light chain, wherein the heavy chain comprises at least one CDR selected from:

a) a CDR1 comprising an amino acid sequence selected from SEQ ID NOs: 9, 17, 25, 33, 41, 49, and 90;

b) a CDR2 comprising an amino acid sequence selected from SEQ ID NOs: 10, 18, 26, 34, 42, and 50; and

c) a CDR3 comprising an amino acid sequence selected from SEQ ID NOs: 11, 19, 27, 35, 43, 51, and 91.

11. The antibody of claim 10, wherein the heavy chain comprises a set comprising a CDR1, a CDR2, and a CDR3, wherein the set is selected from:

a) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 9, a CDR2 having the amino acid sequence of SEQ ID NO: 10, and a CDR3 having the amino acid sequence of SEQ ID NO: 11;

b) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 91;

c) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 17, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 19;

d) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27;

e) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 25, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27;

f) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 91;

g) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 33, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 35;

h) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 41, a CDR2 having the amino acid sequence of SEQ ID NO: 42, and a CDR3 having the amino acid sequence of SEQ ID NO: 43;

i) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 49, a CDR2 having the amino acid sequence of SEQ ID NO: 50, and a CDR3 having the amino acid sequence of SEQ ID NO: 51; and

j) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 57, a CDR2 having the amino acid sequence of SEQ ID NO: 58, and a CDR3 having the amino acid sequence of SEQ ID NO: 59.

12. The antibody of claim 11, wherein the heavy chain comprises a heavy chain variable regions comprising an amino acid sequence selected from SEQ ID NOs: 7, 15, 23, 31, 39, 47, 63, 67, 71, 75, and 79.

13. The antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain and a light chain, wherein the light chain comprises at least one CDR selected from:

a) a CDR1 comprising an amino acid sequence selected from SEQ ID NOs: 12, 20, 28, 36, 44, 52, 60, and 92;

b) a CDR2 comprising an amino acid sequence selected from SEQ ID NOs: 13, 21, 29, 37, 45, 53, 61, and 93; and

c) a CDR3 comprising an amino acid sequence selected from SEQ ID NOs: 14, 22, 30, 38, 46, 54, and 62.

14. The antibody of claim 13, wherein the light chain comprises a set comprising a CDR1, a CDR2, and a CDR3, wherein the set is selected from:

a) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 12, a CDR2 having the amino acid sequence of SEQ ID NO: 13, and a CDR3 having the amino acid sequence of SEQ ID NO: 14;

b) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 22;

c) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 20, a CDR2 having the amino acid sequence of SEQ ID NO: 21, and a CDR3 having the amino acid sequence of SEQ ID NO: 22;

d) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 30;

e) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 28, a CDR2 having the amino acid sequence of SEQ ID NO: 29, and a CDR3 having the amino acid sequence of SEQ ID NO: 30;

f) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 38;

g) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 36, a CDR2 having the amino acid sequence of SEQ ID NO: 37, and a CDR3 having the amino acid sequence of SEQ ID NO: 38;

h) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 44, a CDR2 having the amino acid sequence of SEQ ID NO: 45, and a CDR3 having the amino acid sequence of SEQ ID NO: 46;

i) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 52, a CDR2 having the amino acid sequence of SEQ ID NO: 53, and a CDR3 having the amino acid sequence of SEQ ID NO: 54; and

j) a set comprising a CDR1 having the amino acid sequence of SEQ ID NO: 60, a CDR2 having the amino acid sequence of SEQ ID NO: 61, and a CDR3 having the amino acid sequence of SEQ ID NO: 62.

15. The antibody of claim 14, wherein the light chain comprises a light chain variable regions comprising an amino acid sequence selected from SEQ ID NOs: 8, 16, 24, 32, 40, 48, 56, 65, 69, 73, 77, and 81.

16. The antibody of claim 1, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein:

a) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 9, a CDR2 having the amino acid sequence of SEQ ID NO: 10, and a CDR3 having the amino acid sequence of SEQ ID NO: 11, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 12, a CDR2 having the amino acid sequence of SEQ ID NO: 13, and a CDR3 having the amino acid sequence of SEQ ID NO: 14; or

b) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

c) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 17, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 19, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 20, a CDR2 having the amino acid sequence of SEQ ID NO: 21, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

d) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

e) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 25, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 28, a CDR2 having the amino acid sequence of SEQ ID NO: 29, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

f) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

g) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 33, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 35, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 36, a CDR2 having the amino acid sequence of SEQ ID NO: 37, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

h) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 41, a CDR2 having the amino acid sequence of SEQ ID NO: 42, and a CDR3 having the amino acid sequence of SEQ ID NO: 43, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 44, a CDR2 having the amino acid sequence of SEQ ID NO: 45, and a CDR3 having the amino acid sequence of SEQ ID NO: 46; or

i) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 49, a CDR2 having the amino acid sequence of SEQ ID NO: 50, and a CDR3 having the amino acid sequence of SEQ ID NO: 51, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 52, a CDR2 having the amino acid sequence of SEQ ID NO: 53, and a CDR3 having the amino acid sequence of SEQ ID NO: 54; or

j) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 57, a CDR2 having the amino acid sequence of SEQ ID NO: 58, and a CDR3 having the amino acid sequence of SEQ ID NO: 59, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 60, a CDR2 having the amino acid sequence of SEQ ID NO: 61, and a CDR3 having the amino acid sequence of SEQ ID NO: 62.

17. The antibody of claim 16, wherein:

a) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 7 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 8; or

b) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 15 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 16; or

c) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 71 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 73; or

d) the heavy chain comprises the amino acid sequence of SEQ ID NO: 72 and the light chain comprises the amino acid sequence of SEQ ID NO: 74; or

e) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 23 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 24; or

f) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 75 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 77; or

g) the heavy chain comprises the amino acid sequence of SEQ ID NO: 76 and the light chain comprises the amino acid sequence of SEQ ID NO: 78; or

h) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 31 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 32; or

i) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 79 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 81; or

j) the heavy chain comprises the amino acid sequence of SEQ ID NO: 80 and the light chain comprises the amino acid sequence of SEQ ID NO: 82; or

k) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 39 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 40; or

l) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 67 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 69; or

m) the heavy chain comprises the amino acid sequence of SEQ ID NO: 68 and the light chain comprises the amino acid sequence of SEQ ID NO: 70; or

n) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 47 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 48; or

o) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 55 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 56; or

p) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 63 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 65; or

q) the heavy chain comprises the amino acid sequence of SEQ ID NO: 64 and the light chain comprises the amino acid sequence of SEQ ID NO: 66.

18. A pharmaceutical composition comprising the antibody of any one of the preceding claims.

19. A nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain or a light chain of the antibody of any one of claims 1 to 17.

20. The nucleic acid molecule of claim 19, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

21. The nucleic acid molecule of claim 19 or claim 20, wherein the nucleic acid molecule is a vector.

22. A host cell comprising the nucleic acid molecule of any one of claims 19 to 21.

23. The host cell of claim 22, wherein the host cell comprises a first nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain, and a second nucleic acid molecule comprising a polynucleotide sequence that encodes a light chain.

24. The host cell of claim 22, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

25. A method of producing an antibody of any one of claims 1 to 17 comprising incubating the host cell of claim 23 or claim 24 under conditions sufficient to express the antibody.

26. Use of the pharmaceutical composition of claim 18 in the manufacture of a medicament for stimulating endocortical bone formation in a patient.

27. Use of the pharmaceutical composition of claim 18 in the manufacture of a medicament for treating, managing, or preventing a disease or disorder characterized by bone loss in a patient.

28. The use of claim 27, wherein the disease or disorder is osteoporosis.

29. A single unit dosage form comprising the pharmaceutical composition of claim 18.

CLAIMS

1. A monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) and neutralizes at least one activity of NOTUM, wherein the antibody reduces NOTUM activity in a trisodium 8-octanoyloxypyrene-1,3,6-trisulfonate (OPTS) assay in vitro and reduces NOTUM activity in a Wnt signaling assay in vitro.

2. The antibody of claim 1, wherein the antibody binds to a NOTUM selected from mouse NOTUM, guinea pig NOTUM, cynomolgus monkey NOTUM, and rhesus monkey NOTUM.

3. The antibody of any one of the preceding claims, wherein upon administration to a subject the antibody increases serum PINP levels *in vivo*, increases bone mineral density *in vivo*, increases midshaft femur cortical thickness *in vivo*, increases midshaft femur bone area *in vivo*, increases midshaft humerus cortical thickness *in vivo*, increases endocortical bone formation *in vivo*, increases the proportion of cortical bone volume in the LV5 vertebral body *in vivo*, and/or increases the proportion of femoral neck bone volume to femoral neck total volume *in vivo*.

4. The antibody of any one of the preceding claims, wherein the antibody binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with K_D of less than 50 nM.

5. The antibody of claim 4, wherein the K_D is less than 20 nM.

6. The antibody of claim 5, wherein the K_D is less than 10 nM.

7. The antibody of any one of the preceding claims, wherein the antibody has at least one binding characteristic selected from:

a) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 83 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 84;

b) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 85 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 86;

c) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 94;

d) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 99;

e) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 95 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 2;

f) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO: 8;

g) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 15 and a light chain variable region having the amino acid sequence of SEQ ID NO: 16;

h) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 23 and a light chain variable region having the amino acid sequence of SEQ ID NO: 24;

i) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 31 and a light chain variable region having the amino acid sequence of SEQ ID NO: 32;

j) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 39 and a light chain variable region having the amino acid sequence of SEQ ID NO: 40;

k) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 47 and a light chain variable region having the amino acid sequence of SEQ ID NO: 48; and

l) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 55 and a light chain variable region having the amino acid sequence of SEQ ID NO: 56.

8. The antibody of any one of the preceding claims, wherein the antibody is selected from a mouse antibody, a chimeric antibody, a humanized antibody, and a human antibody.

9. The antibody of claim 1, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein:

a) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 9, a CDR2 having the amino acid sequence of SEQ ID NO: 10, and a CDR3 having the amino acid sequence of SEQ ID NO: 11, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 12, a CDR2 having the amino acid sequence of SEQ ID NO: 13, and a CDR3 having the amino acid sequence of SEQ ID NO: 14; or

b) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

c) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 17, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 19, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 20, a CDR2 having the amino acid sequence of SEQ ID NO: 21, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

d) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

e) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 25, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 28, a CDR2 having the amino acid sequence of SEQ ID NO: 29, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

f) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

g) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 33, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 35, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 36, a CDR2 having the amino acid sequence of SEQ ID NO: 37, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

h) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 41, a CDR2 having the amino acid sequence of SEQ ID NO: 42, and a CDR3 having the

amino acid sequence of SEQ ID NO: 43, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 44, a CDR2 having the amino acid sequence of SEQ ID NO: 45, and a CDR3 having the amino acid sequence of SEQ ID NO: 46; or

i) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 49, a CDR2 having the amino acid sequence of SEQ ID NO: 50, and a CDR3 having the amino acid sequence of SEQ ID NO: 51, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 52, a CDR2 having the amino acid sequence of SEQ ID NO: 53, and a CDR3 having the amino acid sequence of SEQ ID NO: 54; or

j) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 57, a CDR2 having the amino acid sequence of SEQ ID NO: 58, and a CDR3 having the amino acid sequence of SEQ ID NO: 59, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 60, a CDR2 having the amino acid sequence of SEQ ID NO: 61, and a CDR3 having the amino acid sequence of SEQ ID NO: 62.

10. The antibody of claim 9, wherein:

a) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 7 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 8; or

b) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 15 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 16; or

c) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 71 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 73; or

d) the heavy chain comprises the amino acid sequence of SEQ ID NO: 72 and the light chain comprises the amino acid sequence of SEQ ID NO: 74; or

e) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 23 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 24; or

f) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 75 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 77; or

g) the heavy chain comprises the amino acid sequence of SEQ ID NO: 76 and the light chain comprises the amino acid sequence of SEQ ID NO: 78; or

h) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 31 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 32; or

i) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 79 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 81; or

j) the heavy chain comprises the amino acid sequence of SEQ ID NO: 80 and the light chain comprises the amino acid sequence of SEQ ID NO: 82; or

k) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 39 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 40; or

l) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 67 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 69; or

m) the heavy chain comprises the amino acid sequence of SEQ ID NO: 68 and the light chain comprises the amino acid sequence of SEQ ID NO: 70; or

n) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 47 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 48; or

o) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 55 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 56; or

p) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 63 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 65; or

q) the heavy chain comprises the amino acid sequence of SEQ ID NO: 64 and the light chain comprises the amino acid sequence of SEQ ID NO: 66.

11. A pharmaceutical composition comprising the antibody of any one of the preceding claims.

12. A nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain or a light chain of the antibody of any one of claims 1 to 10.

13. The nucleic acid molecule of claim 12, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

14. The nucleic acid molecule of claim 12 or claim 13, wherein the nucleic acid molecule is a vector.

15. A host cell comprising the nucleic acid molecule of any one of claims 12 to 14.

16. The host cell of claim 15, wherein the host cell comprises a first nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain, and a second nucleic acid molecule comprising a polynucleotide sequence that encodes a light chain.

17. The host cell of claim 15, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

18. A method of producing an antibody of any one of claims 1 to 10 comprising incubating the host cell of claim 16 or claim 17 under conditions sufficient to express the antibody.

19. Use of the pharmaceutical composition of claim 11 in the manufacture of a medicament for stimulating endocortical bone formation in a patient.

20. Use of the pharmaceutical composition of claim 11 in the manufacture of a medicament for treating, managing, or preventing a disease or disorder characterized by bone loss in a patient.

21. The use of claim 20, wherein the disease or disorder is osteoporosis.

22. A single unit dosage form comprising the pharmaceutical composition of claim 11.