CLAIMS

What is claimed is:

1. A sclerostin binding agent that cross-blocks the binding of at least one of antibodies Ab-A, Ab-B, Ab-C, Ab-D, Ab-1, Ab-2, Ab-3, Ab-4, Ab-5, Ab-6, Ab-7, Ab-8, Ab-9, Ab-10, Ab-11, Ab-12, Ab-13, Ab-14, Ab-15, Ab-16, Ab-17, Ab-18, Ab-19, Ab-20, Ab-21, Ab-22, Ab-23, and Ab-24 to sclerostin.

2. The sclerostin binding agent of claim 1 wherein said sclerostin binding agent is cross-blocked from binding to sclerostin by at least one of antibodies Ab-A, Ab-B, Ab-C, Ab-D, Ab-1, Ab-2, Ab-3, Ab-4, Ab-5, Ab-6, Ab-7, Ab-8, Ab-9, Ab-10, Ab-11, Ab-12, Ab-13, Ab-14, Ab-15, Ab-16, Ab-17, Ab-18, Ab-19, Ab-20, Ab-21, Ab-22, Ab-23, and Ab-24.

3. A sclerostin binding agent that is cross-blocked from binding to sclerostin by at least one of antibodies Ab-A, Ab-B, Ab-C, Ab-D, Ab-1, Ab-2, Ab-3, Ab-4, Ab-5, Ab-6, Ab-7, Ab-8, Ab-9, Ab-10, Ab-11, Ab-12, Ab-13, Ab-14, Ab-15, Ab-16, Ab-17, Ab-18, Ab-19, Ab-20, Ab-21, Ab-22, Ab-23, and Ab-24.

4. The sclerostin binding agent of claim 1 or 3 wherein the ability of said sclerostin binding agent to cross-block or to be cross-blocked is detected in a Biacore assay.

5. The sclerostin binding agent of claim 1 or 3 wherein the ability of said sclerostin binding agent to cross-block or to be cross-blocked is detected in an ELISA assay.

6. The sclerostin binding agent of claim 1 or 3 wherein said sclerostin binding agent is an antibody.

7. The sclerostin binding agent of claim 1 or 3 wherein said sclerostin binding agent can increase at least one of bone formation, bone mineral density, bone mineral content, bone mass, bone quality and bone strength in a mammal.

8. The sclerostin binding agent of claim 1 or 3 wherein said sclerostin binding agent can block the inhibitory effect of sclerostin in a cell based mineralization assay.

9. A sclerostin binding agent wherein said sclerostin binding agent can block the inhibitory effect of sclerostin in a cell based mineralization assay.

10. A sclerostin binding agent that binds to a Loop 2 epitope.

11. A sclerostin binding agent that binds to a T20.6 epitope.

12. A sclerostin binding agent that binds to a "T20.6 derivative 1 (cystine-knot + 4 arms)" epitope.

13. The sclerostin binding agent of any one of claims 7-12 wherein said sclerostin binding agent is an antibody.

14. A sclerostin binding agent that comprises at least one CDR sequence having at least 75% identity to a CDR selected from SEQ ID NOs:39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 78, 79, 80, 81, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 351, 352, 353, 358, 359, and 360.

15. The sclerostin binding agent of claim 14 comprising at least two of said CDR's.

16. The sclerostin binding agent of claim 14 comprising six of said CDR's.

17. The sclerostin binding agent according to claim 14 wherein said percent identity is 85%.

18. The sclerostin binding agent according to claim 14 wherein said percent identity is 95% .

19. The sclerostin binding agent according to claim 14 comprising:

a) CDR sequences of SEQ ID NOs:39, 40, and 41;
b) CDR sequences of SEQ ID NOs:42, 43, and 44;
c) CDR sequences of SEQ ID NOs:45, 46, and 47;
d) CDR sequences of SEQ ID NOs:48, 49, and 50;
e) CDR sequences of SEQ ID NOs:51, 52, and 53;
f) CDR sequences of SEQ ID NOs:54, 55, and 56;
g) CDR sequences of SEQ ID NOs:57, 58, and 59;
h) CDR sequences of SEQ ID NOs:60, 61, and 62;
i) CDR sequences of SEQ ID NOs:275, 276, and 277;
j) CDR sequences of SEQ ID NOs:287, 288, and 289;
k) CDR sequences of SEQ ID NOs:278, 279, and 280;
l) CDR sequences of SEQ ID NOs:290, 291, and 292;
m) CDR sequences of SEQ ID NOs:78, 79, and 80;
n) CDR sequences of SEQ ID NOs:245, 246, and 247;
o) CDR sequences of SEQ ID NOs:81, 99, and 100;
p) CDR sequences of SEQ ID NOs:248, 249, and 250
q) CDR sequences of SEQ ID NOs:101, 102, and 103;
r) CDR sequences of SEQ ID NOs:251, 252, and 253;

s) CDR sequences of SEQ ID NOs:104, 105, and 106

t) CDR sequences of SEQ ID NOs:254, 255, and 256;

u) CDR sequences of SEQ ID NOs:107, 108, and 109

v) CDR sequences of SEQ ID NOs:257, 258, and 259

w) CDR sequences of SEQ ID NOs:110, 111, and 112;

x) CDR sequences of SEQ ID NOs:260, 261, and 262;

y) CDR sequences of SEQ ID NOs:281, 282, and 283;

z) CDR sequences of SEQ ID NOs:293, 294, and 295;

aa) CDR sequences of SEQ ID NOs:113, 114, and 115;

bb) CDR sequences of SEQ ID NOs:263, 264, and 265;

cc) CDR sequences of SEQ ID NOs:284, 285, and 286;

dd) CDR sequences of SEQ ID NOs:296, 297, and 298;

ee) CDR sequences of SEQ ID NOs:116, 237, and 238;

ff) CDR sequences of SEQ ID NOs:266, 267, and 268;

gg) CDR sequences of SEQ ID NOs:239, 240, and 241;

hh) CDR sequences of SEQ ID NOs:269, 270, and 271;

ii) CDR sequences of SEQ ID NOs:272, 273, and 274;

jj) CDR sequences of SEQ ID NOs:242, 243, and 244;

kk) CDR sequences of SEQ ID NOs:351, 352, and 353; or

ll) CDR sequences of SEQ ID NOs:358, 359, and 360.

20. The sclerostin binding agent according to claim 14 comprising:

a) CDR sequences of SEQ ID NOs:54, 55, and 56 and CDR sequences of SEQ ID NOs:51, 52, and 53;

b) CDR sequences of SEQ ID NOs:60, 61, and 62 and CDR sequences of SEQ ID NOs:57, 58, and 59;

c) CDR sequences of SEQ ID NOs:48, 49, and 50and CDR sequences of SEQ ID NOs:45, 46, and 47;

d) CDR sequences of SEQ ID NOs:42, 43, and 44 and CDR sequences of SEQ ID NOs:39, 40, and 41;

e) CDR sequences of SEQ ID NOs:275, 276, and 277 and CDR sequences of SEQ ID NOs:287, 288, and 289;

f) CDR sequences of SEQ ID NOs:278, 279, and 280 and CDR sequences of SEQ ID NOs:290, 291, and 292;

g) CDR sequences of SEQ ID NOs:78, 79, and 80 and CDR sequences of SEQ ID NOs: 245, 246, and 247;

h) CDR sequences of SEQ ID NOs:81, 99, and 100 and CDR sequences of SEQ ID NOs:248, 249, and 250;

i) CDR sequences of SEQ ID NOs:101, 102, and 103 and CDR sequences of SEQ ID NOs:251, 252, and 253;

j) CDR sequences of SEQ ID NOs:104, 105, and 106 and CDR sequences of SEQ ID NOs:254, 255, and 256;

k) CDR sequences of SEQ ID NOs:107, 108, and 109 and CDR sequences of SEQ ID NOs:257, 258, and 259;

l) CDR sequences of SEQ ID NOs:110, 111, and 112 and CDR sequences of SEQ ID NOs:260, 261, and 262;

m) CDR sequences of SEQ ID NOs:281, 282, and 283 and CDR sequences of SEQ ID NOs:293, 294, and 295;

n) CDR sequences of SEQ ID NOs:113, 114, and 115 and CDR sequences of SEQ ID NOs:263, 264, and 265;

o) CDR sequences of SEQ ID NOs:284, 285, and 286 and CDR sequences of SEQ ID NOs:296, 297, and 298;

p) CDR sequences of SEQ ID NOs:116, 237, and 238 and CDR sequences of SEQ ID NOs:266, 267, and 268;

q) CDR sequences of SEQ ID NOs:239, 240, and 241 and CDR sequences of SEQ ID NOs:269, 270, and 271;

r) CDR sequences of SEQ ID NOs:242, 243, and 244 and CDR sequences of SEQ ID NOs:272, 273, and 274; or

s) CDR sequences of SEQ ID NOs:351, 352, and 353 and CDR sequences of SEQ ID NOs:358, 359, and 360.

21. The sclerostin binding agent of any one of claims 14-20 wherein said sclerostin binding agent is an antibody.

22. A pharmaceutical composition comprising a sclerostin binding agent according to any one of claims 1-12 and 14-20.

23. The composition of claim 22 wherein said sclerostin binding agent is an antibody.

24. A sclerostin binding agent comprising at least one CDR sequence having at least 75% identity to a CDR selected from SEQ ID NOs:245, 246, 247, 78, 79, 80, 269, 270,

271, 239, 240 and 241.

25. A sclerostin binding agent comprising at least one CDR sequence having at least 75% identity to a CDR selected from CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2 and CDR-L3 wherein CDR-H1 has the sequence given in SEQ ID NO:245 or SEQ ID NO:269, CDR-H2 has the sequence given in SEQ ID NO:246 or SEQ ID NO:270, CDR-H3 has the sequence given in SEQ ID NO:247 or SEQ ID NO:271, CDR-L1 has the sequence given in SEQ ID NO:78 or SEQ ID NO:239, CDR-L2 has the sequence given in SEQ ID NO:79 or SEQ ID NO:240 and CDR-L3 has the sequence given in SEQ ID NO:80 or SEQ ID NO 241.

26. A sclerostin binding agent according to claim 25 comprising three CDRs, CDR-H1, CDR-H2 and CDR-H3 wherein

(a) CDR-H1 is SEQ ID NO:245, CDR-H2 is SEQ ID NO:246 and CDR-H3 is SEQ ID NO:247 or

(b) CDR-H1 is SEQ ID NO:269, CDR-H2 is SEQ ID NO:270 and CDR-H3 is SEQ ID NO:271.

27. A sclerostin binding agent according to claim 25 comprising three CDRs, CDR-L1, CDR-L2 and CDR-L3 wherein

(a) CDRL1 is SEQ ID NO:78, CDR-L2 is SEQ ID NO:79 and CDR-L3 is SEQ ID NO:80; or

(b) CDRL1 is SEQ ID NO:239, CDR-L2 is SEQ ID NO:240 and CDR-L3 is SEQ ID NO:241.

28. A sclerostin binding agent according to claim 25 comprising six CDRs, CDRH-1, CDR-H2, CDR-H3, CDR-L1 CDR-L2 and CDR-L3 wherein

(a) CDR-H1 is SEQ ID NO:245, CDR-H2 is SEQ ID NO:246, CDR-H3 is SEQ ID NO:247, CDR-L1 is SEQ ID NO:78, CDR-L2 is SEQ ID NO:79 and CDR-L3 is SEQ ID NO:80; or

(b) CDR-H1 is SEQ ID NO:269, CDR-H2 is SEQ ID NO:270, CDR-H3 is SEQ ID NO:271, CDR-L1 is SEQ ID NO:239, CDR-L2 is SEQ ID NO:240 and CDR-L3 is SEQ ID NO:241.

29. The sclerostin binding agent of any one of claims 24-28 which is an antibody.

30. The sclerostin binding agent of claim 29 comprising a heavy chain wherein said heavy chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:333; SEQ ID NO:378; SEQ ID NO:327; SEQ ID NO:329; or SEQ ID NO:366.

31. The sclerostin binding agent of claim 29 comprising a light chain wherein said light chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:332; SEQ ID NO:376; SEQ ID NO:314; SEQ ID NO:328; or SEQ ID NO:364.

32. The sclerostin binding agent of claim 29 comprising both a heavy chain and a light chain wherein

(a) the heavy chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:333 and the light chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:332; or

(b) the heavy chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:378 and the light chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:376; or

(c) the heavy chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:327 and the light chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:314; or

(d) the heavy chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:329 and the light chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:328; or

(c) the heavy chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:366 and the light chain comprises a polypeptide having at least 85% identity to the sequence given in SEQ ID NO:364.

33. The sclerostin binding agent of any one of claims 24-32 which comprises a light chain and/or heavy chain constant region.

34. The sclerostin binding agent of claim 33 which comprises the IgG4 or the IgG2 constant region.

35. A sclerostin binding agent having a heavy chain comprising CDR's H1, H2 and H3 and comprising a polypeptide having the sequence provided in SEQ ID NO:137 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:245, 246 and 247, respectively, and a light chain comprising CDR's L1, L2 and L3 and comprising a polypeptide having the sequence provided in SEQ ID NO:133 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:78, 79 and 80, respectively.

36. A sclerostin binding agent having a heavy chain comprising CDR's H1, H2 and H3 and comprising a polypeptide having the sequence provided in SEQ ID NO:145 or 392 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:245, 246 and 247, respectively, and a light chain comprising CDR's L1, L2 and L3 and comprising a

polypeptide having the sequence provided in SEQ ID NO:141 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:78, 79 and 80, respectively.

37. A sclerostin binding agent having a heavy chain comprising CDR's H1, H2 and H3 and comprising a polypeptide having the sequence provided in SEQ ID NO:335 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:269, 270 and 271, respectively, and a light chain comprising CDR's L1, L2 and L3 and comprising a polypeptide having the sequence provided in SEQ ID NO:334 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:239, 240 and 241, respectively.

38. A sclerostin binding agent having a heavy chain comprising CDR's H1, H2 and H3 and comprising a polypeptide having the sequence provided in SEQ ID NO:331 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:269, 270 and 271, respectively, and a light chain comprising CDR's L1, L2 and L3 and comprising a polypeptide having the sequence provided in SEQ ID NO:330 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:239, 240 and 241, respectively.

39. A sclerostin binding agent having a heavy chain comprising CDR's H1, H2 and H3 and comprising a polypeptide having the sequence provided in SEQ ID NO:345 or 396 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:269, 270 and 271, respectively, and a light chain comprising CDR's L1, L2 and L3 and comprising a polypeptide having the sequence provided in SEQ ID NO:341 or a variant thereof in which said CDR's are at least 75% identical to SEQ ID NO:239, 240 and 241, respectively.

40. A sclerostin binding agent having a heavy chain comprising a polypeptide having the sequence provided in SEQ ID NO:137, and a light chain comprising a polypeptide having the sequence provided in SEQ ID NO:133.

41. A sclerostin binding agent having a heavy chain comprising a polypeptide having the sequence provided in SEQ ID NO:145 or 392, and a light chain comprising a polypeptide having the sequence provided in SEQ ID NO: 141.

42. A sclerostin binding agent having a heavy chain comprising a polypeptide having the sequence provided in SEQ ID NO:335, and a light chain comprising a polypeptide having the sequence provided in SEQ ID NO:334.

43. A sclerostin binding agent having a heavy chain comprising a polypeptide having the sequence provided in SEQ ID NO:331, and a light chain comprising a polypeptide having the sequence provided in SEQ ID NO:330.

44. A sclerostin binding agent having a heavy chain comprising a polypeptide having the sequence provided in SEQ ID NO:345 or 396, and a light chain comprising a polypeptide having the sequence provided in SEQ ID NO:341.

45. A sclerostin binding agent according to any one of claims 24-44 to which one or more effector or reporter molecule(s) is attached.

46. An isolated polynucleotide sequence encoding the sclerostin binding agent according to any one of claims 24-44.

47. A cloning or expression vector comprising one or more polynucleotide sequences according to claim 46.

48. A vector according to claim 47, wherein the vector comprises at least one sequence given in SEQ ID NQ:134, 136, 138, 140, 142, 144, 146, 148, 308, 310, 312, 342, 344, 346, 348, 349, 365, 367, 373, 375, and 379.

49. A host cell comprising one or more cloning or expression vectors according to claim 47 or claim 48.

50. A process for the production of the sclerostin binding agent of any one of claims 24-44, comprising culturing the host cell of claim 49 and isolating the sclerostin binding agent.

51. A pharmaceutical composition comprising a sclerostin binding agent according to any one of claims 24-45 in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier.

52. A pharmaceutical composition according to claim 51, additionally comprising other active ingredients.

53. A sclerostin binding agent according to any one of claims 24-45 or a pharmaceutical composition according to claim 51 or claim 52, for use in the treatment or prophylaxis of a pathological disorder that is mediated by sclerostin or that is associated with an increased level of sclerostin.

54. Use of a sclerostin binding agent according to any one of claims 1-12 and 14-20 for the preparation of a pharmaceutical composition for treating a bone-related disorder in a mammal.

55. The use according to claim 54, wherein the sclerostin binding agent is an antibody.

56. Use of a sclerostin binding agent according to any one of claims 24-45 in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier for the preparation of a pharmaceutical composition for treating a bone-related disorder in a mammal.

57. The use according to any one of claims 54-56, wherein the bone-related disorder is at least one of achondroplasia, cleidocranial dysostosis, enchondromatosis, fibrous dysplasia, Gaucher's Disease, hypophosphatemic rickets, Marfan's syndrome, multiple hereditary exotoses, neurofibromatosis, osteogenesis imperfecta, osteopetrosis, osteopoikilosis, sclerotic lesions, pseudoarthrosis, pyogenic osteomyelitis, periodontal disease, anti-epileptic drug induced bone loss, primary and secondary hyperparathyroidism, familial hyperparathyroidism syndromes, weightlessness induced bone loss, osteoporosis in men, postmenopausal bone loss, osteoarthritis, renal osteodystrophy, infiltrative disorders of bone, oral bone loss, osteonecrosis of the jaw, juvenile Paget' s disease, melorheostosis, metabolic bone diseases, mastocytosis, sickle cell anemia/disease, organ transplant related bone loss, kidney transplant related bone loss, systemic lupus erythematosus, ankylosing spondylitis, epilepsy, juvenile arthritides, thalassemia, mucopolysaccharidoses, Fabry Disease, Turner Syndrome, Down Syndrome, Klinefelter Syndrome, leprosy, Perthes' Disease, adolescent idiopathic scoliosis, infantile onset multi-system inflammatory disease, Winchester Syndrome, Menkes Disease, Wilson's Disease, ischemic bone disease (such as Legg-Calve-Perthes disease, regional migratory osteoporosis), anemic states, conditions caused by steroids, glucocorticoid-induced bone loss, heparin-induced bone loss, bone marrow disorders, scurvy, malnutrition, calcium deficiency, osteoporosis, osteopenia, alcoholism, chronic liver disease, postmenopausal state, chronic inflammatory conditions, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, inflammatory colitis, Crohn's disease, oligomenorrhea, amenorrhea, pregnancy, diabetes mellitus, hyperthyroidism, thyroid disorders, parathyroid disorders, Cushing's disease, acromegaly, hypogonadism, immobilization or disuse, reflex sympathetic dystrophy syndrome, regional osteoporosis, osteomalacia, bone loss associated with joint replacement, HIV associated bone loss, bone loss associated with loss of growth hormone, bone loss associated with cystic fibrosis, chemotherapy associated bone loss, tumor induced bone loss, cancer-related bone loss, hormone ablative bone loss, multiple myeloma, drug-induced bone loss, anorexia nervosa, disease associated facial bone loss, disease associated cranial bone loss, disease associated bone loss of the jaw, disease associated bone loss of the skull, bone loss associated with aging, facial bone loss associated with aging, cranial bone loss associated with aging, jaw bone loss associated with aging, and skull bone loss associated with aging and bone loss associated with space travel.

58. Use of a sclerostin binding agent according to any one of claims 1-12 and 14-20 for the preparation of a pharmaceutical composition for increasing at least one of bone formation, bone mineral content, bone mass, bone mineral density, bone quality, and bone strength in a mammal.

59. The use according to claim 58, wherein the sclerostin binding agent is an antibody.

60. Use of a sclerostin binding agent according to any one of claims 24-45 in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier for the preparation of a pharmaceutical composition for increasing at least one of bone formation, bone mineral content, bone mass, bone mineral density, bone quality, and bone strength in a mammal.

61. Use of a sclerostin binding agent according to any one of claims 1-12 and 14-20 for the preparation of a pharmaceutical composition for improving the outcome in a mammal undergoing one or more of an orthopedic procedure, dental procedure, implant surgery, joint replacement, bone grafting, bone cosmetic surgery and bone repair such as fracture healing, nonunion healing, delayed union healing and facial reconstruction, wherein the pharmaceutical composition is for administration to said mammal before, during and/or after said procedure, replacement, graft, surgery or repair.

62. The use according to claim 61, wherein the sclerostin binding agent is an antibody.

63. Use of a sclerostin binding agent according to any one of claims 24-45 in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier for the preparation of a pharmaceutical composition for for improving the outcome in a mammal undergoing one or more of an orthopedic procedure, dental procedure, implant surgery, joint replacement, bone grafting, bone cosmetic surgery and bone repair such as fracture healing, nonunion healing, delayed union healing and facial reconstruction, wherein the pharmaceutical composition is for administration to said mammal before, during and/or after said procedure, replacement, graft, surgery or repair.

64. An antibody, wherein said antibody is Ab-A, Ab-B, Ab-C, Ab-D, Ab-1, Ab-2, Ab-3, Ab-4, Ab-5, Ab-6, Ab-7, Ab-8, Ab-9, Ab-I0, Ab-I 1, Ab-12, Ab-13, Ab-14, Ab-15, Ab-16, Ab-17, Ab-18, Ab-19, Ab-20, Ab-21, Ab-22, Ab-23, or Ab-24.

65. A diagnostic kit comprising a sclerostin binding agent according to any one of claims 1, 3, 9-12 and 14-20.

66. A diagnostic kit comprising an antibody according to claim 6.

67. A diagnostic kit comprising an antibody according to claim 21.

68. A diagnostic kit comprising an antibody according to claim 29.

69. A polypeptide comprising at least one of SEQ ID NOs:39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 78, 79, 80, 81, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 351, 352, 353, 358, 359, and 360.

70. A polypeptide according to claim 69 conjugated to at least one of Fc, PEG, albumin, and transferrin.

CLAIMS

What is claimed is:

1. A sclerostin-binding antibody comprising the following CDR sequences:

CDR-H1: DYNMH (SEQ ID NO:245);

CDR-H2: EINPNSGGAGYNQKFKG (SEQ ID NO:246);

CDR-H3: LGYDDIYDDWYFDV (SEQ ID NO:247);

CDR-L1: RASQDISNYLN (SEQ ID NO:78);

CDR-L2: YTSRLLS (SEQ ID NO:79); and

CDR-L3: QQGDTLPYT (SEQ ID NO:80).

2. The sclerostin-binding antibody of claim 1 comprising a heavy chain comprising a polypeptide sequence having at least 85% identity to the sequence of SEQ ID NO: 378.

3. The sclerostin-binding antibody of claim 1 or 2 comprising a light chain comprising a polypeptide sequence having at least 85% identity to the sequence of SEQ ID NO: 376.

4. The sclerostin-binding antibody of any one of claims 1 to 3 comprising both a heavy chain comprising a polypeptide sequence having at least 85% identity to the sequence of SEQ ID NO: 378 and a light chain comprising a polypeptide sequence having at least 85% identity to the sequence of SEQ ID NO: 376.

5. The sclerostin-binding antibody of any one of claims 1 to 4, which comprises a light chain and/or heavy chain constant region.

6. The sclerostin-binding antibody of claim 5, which is an IgG.

7. The sclerostin-binding antibody of claim 5, which comprises the human IgG4 or the human IgG2 constant region.

8. The sclerostin-binding antibody of claim 1 having heavy chains of SEQ ID NO: 137 and light chains of SEQ ID NO: 133.

9. The sclerostin-binding antibody of claim 1 having heavy chains of SEQ ID NO: 145 or 392 and light chains of SEQ ID NO: 141.

10. The sclerostin-binding antibody of any one of the claims 1 to 4, wherein said antibody is a sclerostin-binding antibody fragment comprising the six CDRs set forth in claim 1.

11. The sclerostin-binding antibody of any one of claims 1 to 9, which is a complete antibody.

12. The sclerostin-binding antibody of claim 10, wherein said antibody is an $F(ab')_2$, Fab, Fab' or Fv fragment.

13. The sclerostin-binding antibody of any one of claims 1 to 7, which is a humanized antibody or a chimeric antibody.

14. The sclerostin-binding antibody of any one of the preceding claims, wherein said antibody has a dissociation constant for human sclerostin as measured by surface plasmon resonance of less than or equal to 1×10^{-9} M, less than or equal to 1×10^{-10} M, less than or equal to 1×10^{-11} M, or less than or equal to 1×10^{-12} M.

15. A sclerostin-binding antibody of any one of the preceding claims to which one or more effector or reporter molecule(s) is attached.

16. The sclerostin-binding antibody of any one of the preceding claims, wherein said antibody can increase at least one of bone formation, bone mineral density, bone mineral content, bone mass, bone quality and bone strength in a mammal.

17. The sclerostin-binding antibody of any one of any one of the preceding claims, wherein said antibody can block the inhibitory effect of sclerostin in a cell-based mineralization assay.

18. An isolated polynucleotide sequence encoding the sclerostin-binding antibody according to any one of claims 1 to 17.

19. A cloning or expression vector comprising one or more polynucleotide sequences according to claim 18.

20. The vector of claim 19, wherein the vector comprises at least one sequence given in SEQ ID NO: 134, 136, 138, 140, 142, 144, 146, 148 and 379.

21. A host cell comprising one or more cloning or expression vectors according to claim 19 or claim 20.

22. A process for the production of the sclerostin-binding antibody of any one of claims 1 to 17, comprising culturing the host cell of claim 21 and isolating the sclerostin-binding antibody.

23. A pharmaceutical composition comprising a sclerostin-binding antibody according to any one of claims 1 to 17 in combination with one or more of a pharmaceutically acceptable excipient, diluent and carrier.

24. The pharmaceutical composition of claim 23, additionally comprising other active ingredients.

25. The sclerostin-binding antibody of any one of claims 1 to 17 or the pharmaceutical composition of claim 23 or claim 24, for use in the method of treatment of a bone disorder associated with at least one of low bone formation, low bone mineral density, low bone mineral content, low bone mass, low bone quality and low bone strength in a mammalian subject, which method comprises providing to a subject in need of such treatment an amount of said antibody sufficient to increase at least one of bone formation, bone mineral density, bone mineral content, bone mass, bone quality and bone strength.

26. The antibody or pharmaceutical composition according to claim 25 for said use, wherein the bone disorder is osteopenia, osteoporosis, bone loss or abnormal growth or development of bone caused by at least one of achondroplasia, cleidocranial dysostosis, enchondromatosis, fibrous dysplasia, Gaucher's Disease, hypophosphatemic rickets, Marfan's syndrome, multiple hereditary exotoses, neurofibromatosis, osteogenesis imperfecta, osteopoikilosis, sclerotic lesions, pseudoarthrosis, pyogenic osteomyelitis, periodontal disease, anti-epileptic drug

induced bone loss, primary and secondary hyperparathyroidism, familial hyperparathyroidism syndromes, weightlessness induced bone loss, osteoporosis in men, postmenopausal bone loss, osteoarthritis, renal osteodystrophy, infiltrative disorders of bone, oral bone loss, osteonecrosis of the jaw, juvenile Paget's disease, melorheostosis, metabolic bone diseases, mastocytosis, sickle cell anemia/disease, organ transplant related bone loss, kidney transplant related bone loss, systemic lupus erythematosus, ankylosing spondylitis, epilepsy, juvenile arthritides, thalassemia, mucopolysaccharidoses, Fabry Disease, Turner Syndrome, Down Syndrome, Klinefelter Syndrome, leprosy, Perthes' Disease, adolescent idiopathic scoliosis, infantile onset multi-system inflammatory disease, Winchester Syndrome, Menkes Disease, Wilson's Disease, ischemic bone disease (such as Legg-Calve-Perthes disease, regional migratory osteoporosis), anemic states, conditions caused by steroids, glucocorticoid-induced bone loss, heparin-induced bone loss, bone marrow disorders, scurvy, malnutrition, calcium deficiency, alcoholism, chronic liver disease, postmenopausal state, chronic inflammatory conditions, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, inflammatory colitis, Crohn's disease, oligomenorrhea, amenorrhea, pregnancy, diabetes mellitus, hyperthyroidism, thyroid disorders, parathyroid disorders, Cushing's disease, acromegaly, hypogonadism, immobilization or disuse, reflex sympathetic dystrophy syndrome, regional osteoporosis, osteomalacia, bone loss associated with joint replacement, HIV associated bone loss, bone loss associated with loss of growth hormone, bone loss associated with cystic fibrosis, chemotherapy associated bone loss, tumor induced bone loss, cancer-related bone loss, hormone ablative bone loss, multiple myeloma, drug-induced bone loss, anorexia nervosa, disease associated facial bone loss, disease associated cranial bone loss, disease associated bone loss of the jaw, disease associated bone loss of the skull, bone loss associated with aging, facial bone loss associated with aging, cranial bone loss associated with aging, jaw bone loss associated with aging, skull bone loss associated with aging and bone loss associated with space travel.

27. The antibody or pharmaceutical composition of claim 25 for said use, wherein the bone disorder is osteoporosis.

28. The antibody of any one of claims 1 to 17 or the pharmaceutical composition of claim 23 or 24, for use in a method of improving the outcome in a mammal undergoing one or more of an orthopedic procedure, dental procedure, implant surgery, joint replacement, bone grafting, bone cosmetic surgery and bone repair such as fracture healing, nonunion healing, delayed union healing and facial reconstruction, said method comprising administering said antibody or composition to said mammal before, during and/or after said procedure, replacement, graft, surgery or repair.

29. A diagnostic kit comprising the antibody of any one of claims 1 to 17.

30. Use of the antibody of any one of claims 1 to 17 for the manufacture of a medicament for treatment of a bone disorder associated with at least one of low bone formation, low bone mineral density, low bone mineral content, low bone mass, low bone quality and low bone strength in a mammalian subject.

31. The use of claim 30, wherein the bone disorder is osteopenia, osteoporosis, bone loss or abnormal growth or development of bone caused by at least one of achondroplasia, cleidocranial dysostosis, enchondromatosis, fibrous dysplasia, Gaucher's Disease, hypophosphatemic rickets, Marfan's syndrome, multiple hereditary exotoses, neurofibromatosis, osteogenesis imperfecta, osteopetrosis, osteopoikilosis, sclerotic lesions, pseudoarthrosis, pyogenic osteomyelitis, periodontal disease, anti-epileptic drug induced bone loss, primary and secondary hyperparathyroidism, familial hyperparathyroidism syndromes, weightlessness induced bone loss, osteoporosis in men, postmenopausal bone loss, osteoarthritis, renal osteodystrophy, infiltrative disorders of bone, oral bone loss, osteonecrosis of the jaw, juvenile Paget's disease, melorheostosis, metabolic bone diseases, mastocytosis, sickle cell anemia/disease, organ transplant related bone loss, kidney transplant related bone loss, systemic lupus erythematosus, ankylosing spondylitis, epilepsy, juvenile arthritides, thalassemia, mucopolysaccharidoses, Fabry Disease, Turner Syndrome, Down Syndrome, Klinefelter Syndrome, leprosy, Perthes' Disease, adolescent idiopathic scoliosis, infantile onset multi-system inflammatory disease, Winchester Syndrome, Menkes Disease, Wilson's Disease, ischemic bone disease (such as Legg-Calve-Perthes disease, regional migratory osteoporosis),

anemic states, conditions caused by steroids, glucocorticoid-induced bone loss, heparin-induced bone loss, bone marrow disorders, scurvy, malnutrition, calcium deficiency, alcoholism, chronic liver disease, postmenopausal state, chronic inflammatory conditions, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, inflammatory colitis, Crohn's disease, oligomenorrhea, amenorrhea, pregnancy, diabetes mellitus, hyperthyroidism, thyroid disorders, parathyroid disorders, Cushing's disease, acromegaly, hypogonadism, immobilization or disuse, reflex sympathetic dystrophy syndrome, regional osteoporosis, osteomalacia, bone loss associated with joint replacement, HIV associated bone loss, bone loss associated with loss of growth hormone, bone loss associated with cystic fibrosis, chemotherapy associated bone loss, tumor induced bone loss, cancer-related bone loss, hormone ablative bone loss, multiple myeloma, drug-induced bone loss, anorexia nervosa, disease associated facial bone loss, disease associated cranial bone loss, disease associated bone loss of the jaw, disease associated bone loss of the skull, bone loss associated with aging, facial bone loss associated with aging, cranial bone loss associated with aging, jaw bone loss associated with aging, skull bone loss associated with aging and bone loss associated with space travel.

32. The use of claim 30, wherein the bone disorder is osteoporosis.

33. Use of the antibody of any one of claims 1 to 17 for the manufacture of a medicament for improving the outcome in a mammal undergoing one or more of an orthopedic procedure, dental procedure, implant surgery, joint replacement, bone grafting, bone cosmetic surgery and bone repair such as fracture healing, nonunion healing, delayed union healing and facial reconstruction, wherein the medicament is for administering to said mammal before, during and/or after said procedure, replacement, graft, surgery or repair.