BACKGROUND OF THE INVENTION

[0005] Periodontal infections and gingival inflammations are known to be major causes of periodontal diseases. Both are chronic inflammatory diseases, and as they progress, the periodontal tissue is destroyed and the alveolar bone is reduced due to bone resorption causing loss of tooth support in some cases. In addition, the alveolar bone may become defective due to perforations caused by surgical treatments or apical lesions from progressed dental caries.

SUMMARY OF THE INVENTION

[0006] The invention is directed to methods of using a sclerostin inhibitor to enhance alveolar bone. In one aspect, the present invention refers to an anti-sclerostin antibody for use in treating alveolar bone loss by increasing alveolar bone height, wherein the anti-sclerostin antibody crossblocks or is crossblocked by an anti-sclerostin antibody that binds to a sub-region of SEQ ID NO: 1 comprising SEQ ID NO: 2 (DVSEYSCRELHFTR; corresponding to amino acids 51-64 of SEQ ID NO: 1), SEQ ID NO: 3 (SAKPVTELVCSGQCGPAR; corresponding to amino acids 73-90 of SEQ ID NO: 1), SEQ ID NO: 4 (WWRPSGPDFRCIPDRYR; corresponding to amino acids 101-117 of SEQ ID NO: 1) and SEQ ID NO: 5 (LVASCKCKRLTR; corresponding to amino acids 138-149 of SEQ ID NO: 1); wherein the anti-sclerostin antibody comprises a) CDR sequences of SEQ ID NOs:48, 49, and 50 and CDR sequences of SEQ ID NOs:45, 46, and 47; b) CDR sequences of SEQ ID NOs:42, 43, and 44 and CDR sequences of SEQ ID NOs:39, 40, and 41; c) CDR sequences of SEQ ID NOs:275, 276, and 277 and CDR sequences of SEQ ID NOs:287, 288, and 289;d) CDR sequences of SEQ ID NOs:278, 279, and 280 and CDR sequences of SEQ ID NOs:290, 291, and 292;e) CDR sequences of SEQ ID NOs:281, 282, and 283 and CDR sequences of SEQ ID NOs:293, 294, and 295;f) CDR sequences of SEQ ID NOs:284, 285, and 286 and CDR sequences of SEQ ID NOs:296, 297, and 298; g) CDR sequences of SEQ ID NOs:116, 237, and 238 and CDR sequences of SEQ ID NOs:266, 267, and 268; or h) CDR sequences of SEQ ID NOs:242, 243, and 244 and CDR sequences of SEQ ID NOs:272, 273, and 274. In one example, described herein is a method of treating alveolar bone loss in a subject comprising administering a sclerostin inhibitor (e.g., an anti-sclerostin antibody or antibody fragment) in an amount effective to decrease the distance between the cement-enamel junction and the alveolar bone crest, optionally at a dose from about 5 mg to about 1,000 mg per week. In one example, the sclerostin inhibitor is administered twice a week for the duration of the treatment period. In another example, the sclerostin inhibitor is administered once a week for the duration of the treatment period.

[0007] The treatment period can be at least about 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 3 months, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 4 months, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 5 months, 21 weeks, 22 weeks, 23 weeks, 24 weeks, 6 months, 25 weeks, 26 weeks, 27 weeks 28 weeks, 7 months, 29 weeks, 30 weeks, 31 weeks or longer (e.g., 8 months, 9 months, 10 months, 11 months, 1 year, 15 months, 18 months or longer). In some examples, the treatment period is about 6-12 weeks. In some examples, the treatment period is 4-12 weeks, or about 1-3 months. In some examples, the treatment period is about 12-20 weeks, or about 3-5 months. In some examples, the treatment period is about 20-32 weeks, or about 5-8 months. In some examples, the treatment period is about 24-36 weeks, or about 6-9 months. In some examples, the treatment period is no more than about 28 weeks. In some examples, the treatment period is about 1 year. In some or any examples, the treatment period is no more than about 18 months.

[0008] In some or any examples, the distance between the cement-enamel junction and the alveolar bone crest is decreased by at least 10% (e.g., at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or more) compared to the pre-treatment distance by six weeks after initiation of treatment. In

some or any examples, the distance between the cement-enamel junction and the alveolar bone crest is decreased by at least 10% (e.g., at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or more) compared to a control subject (i.e., a subject with advanced periodontal disease that did not receive treatment with the sclerostin inhibitor) by six weeks after initiation of treatment. In some examples, the distance between the cement-enamel junction and the alveolar bone crest is restored to the pre-disease state by six weeks after initiation of treatment. In some examples, the distance between the cement-enamel junction and the alveolar bone crest is less than or equal to about 2 mm (e.g., about 2 mm, about 1.9 mm, about 1.8 mm, about 1.7 mm, about 1.6 mm, about 1.5 mm, about 1.4 mm, about 1.3 mm, about 1.2 mm, about 1.1 mm or about 1 mm) by six weeks after initiation of treatment.

[0009] In some or any examples, the alveolar bone height is increased by at least 10% (e.g., at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or more) compared to the pre-treatment alveolar bone height by six weeks after initiation of treatment. In some or any examples, the alveolar bone height is increased by at least 10% (e.g., at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or more) compared to a control subject (i.e., a subject with advanced periodontal disease that did not receive treatment with the sclerostin inhibitor) by six weeks after initiation of treatment. In some examples, the alveolar bone height is restored to pre-disease state alveolar bone height by six weeks after initiation of treatment.

[0010] In some or any examples, the alveolar bone height is increased by at least 0.1 mm (e.g., at least about 0.1 mm, about 0.2 mm, about 0.3 mm, about 0.4 mm, about 0.5 mm, about 0.6 mm, about 0.7 mm, about 0.8 mm, about 0.9 mm, about 1 mm, about 1.5 mm, about 2 mm, about 2.5 mm, about 3 mm, about 3.5 mm, about 4 mm, about 4.5 mm, about 5 mm, about 5.5 mm, about 6 mm, about 6.5 mm, about 7 mm, about 7.5 mm, about 8 mm, about 8.5 mm, about 9 mm, about 9.5, or about 10 mm) or more compared to pre-treatment alveolar bone height or compared to a control subject (i.e., a subject with advanced periodontal disease that did not receive treatment with the sclerostin inhibitor) by six weeks after initiation of treatment.

[0011] In some or any examples, the alveolar bone density is increased by at least 10% (e.g., at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or more) compared to the pre-treatment alveolar bone density or compared to a control subject (i.e., a subject with advanced periodontal disease that did not

receive treatment with the sclerostin inhibitor) by six weeks after initiation of treatment. In some examples, the alveolar bone density is restored to pre-disease state by six weeks after initiation of treatment.

[0012] In some or any examples, the alveolar bone volume fraction (BVF) is increased by at least 10% (e.g., at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or more) compared to the pre-treatment alveolar BVF or compared to a control subject (i.e., a subject with advanced periodontal disease that did not receive treatment with the sclerostin inhibitor) by six weeks after initiation of treatment.

[0013] In some or any examples, the methods described herein may further comprise measuring the bone mineral density of the alveolar bone prior to the administration of the sclerostin inhibitor (e.g., anti-sclerostin antibody or antibody fragment) to identify subjects in need of treatment with the sclerostin inhibitor. Subjects presenting with alveolar bone density measurements of less than about 750 Hounsfield Units (e.g., about 750 HU, about 700 HU, about 650 HU, about 600 HU, about 550 HU, about 500 HU, about 450 HU, about 400 HU or less) are identified as subjects in need of treatment with the anti-sclerostin antibody or antibody fragment.

[0014] The alveolar bone loss for treatment by the methods described herein includes, but is not limited to, alveolar bone loss associated with periodontitis (e.g., advanced periodontal disease), tooth loss, tooth extraction, denture wearing, oral surgery, osteolmyelitis, osteoradionecrosis, developmental deformities (e.g., defects at birth such as missing portions of the teeth, facial bones or jaw), sinus deficiencies, misalignment, or trauma (e.g., avulsed tooth or jaw fracture). In some examples, the subject to be treated is suffering from advanced periodontitis.

[0015] In some examples, the alveolar bone loss is produced by removal of sections of bone containing a tumor (e.g. benign tumor). Exemplary benign bone tumors include, but are not limited to, osteoma, osteoid osteoma, osteoblastoma, osteochondroma, enchondroma, chonrdomyxoid fibroma, aneurysmal bone cyst, unicameral bone cyst, fibrous dysplasia of bone, and giant cell tumor of the bone.

[0016] In some or any examples, the sclerostin inhibitor (e.g. anti-sclerostin antibody or antibody fragment) is administered in combination with the use of materials that support the regrowth of bone such as bone graft, bone dust, bone chips, demineralized bone matrix, bone scaffolds, prosthesis, metal stabilizers, or bone scaffold substances comprising one or

more of polymers, ceramics, cement and calcium phosphates-based bone-graft substitutes. Many variations of such materials are known in the art.

[0017] In some or any examples, the method comprises administering a standard of care therapy for the treatment of the periodontal disease to the subject prior to administering the sclerostin inhibitor (e.g., anti-sclerostin antibody or antibody fragment). For example, in some examples, the standard of care therapy for the treatment of periodontal disease is a therapeutic, including but not limited to, Periostat® and/or chemically modified tetracycline-3 (CMT-3). In some examples, the standard of care therapy comprises oral irrigation and/or scaling and supra- and/or sub-gingival debridement (e.g., removal of microbial plaque and calculus) of the affected area of the subject. In some examples, the standard of care comprises performing oral irrigation and/or scaling and debridement of the affected area in combination with Periostat and/or CMT-3 prior to administration of the sclerostin inhibitor. In some examples, the method comprises administering the standard of care therapy concurrently with the administration of the sclerostin inhibitor. In other examples, the standard of care therapy is administered sequentially. For example, the standard of care therapy can be administered 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, 12 weeks or more prior to administering the sclerostin inhibitor to the subject. In preferred examples, the periodontal disease progression in the subject is slowed, halted or reversed prior to administration of the sclerostin inhibitor.

[0018] In some or any examples, the method further comprises administering an antibiotic, such as an antibiotic selected from the group consisting of amoxicillin, tetracycline hydrochloride, doxycycline, minocycline, azithromycin, roxithromycin, moxifloxacin, ciprofloxacin and metronidazole. In some examples, the method comprises administering the antibiotic to the subject prior to administering or after administering the sclerostin inhibitor to the subject. In other examples, the method comprises administering the antibiotic to the subject concurrently with the administration of the sclerostin inhibitor.

[0019] In some or any examples, the method further comprises administering a second bone-enhancing therapeutic for the treatment of decreased bone mineral density or bone fracture. Many therapeutics of this type are known in the art. In some examples, the bone-enhancing therapeutic is selected from the group consisting of an anti-resorptive drug, a bone-forming agent, an estrogen receptor modulator (including, but not limited to, raloxifene, bazedoxifene and lasofoxifene) and a drug that has an inhibitory effect on osteoclasts. In some examples, the second bone-enhancing agent is selected from the group consisting

of, a bisphosphonate (including, but not limited to, alendronate sodium (FOSAMAX®), risedronate, ibandronate sodium (BONIVA®) and zoledronic acid (RECLAST®)), an estrogen or estrogen analogue, a calcium source, Tibolone, calcitonin, a calcitriol and hormone replacement therapy. In some examples, the second bone-enhancing agent includes, but is not limited to parathyroid hormone (PTH) or a peptide fragment thereof, PTH-related protein (PTHrp), bone morphogenetic protein, osteogenin, NaF, a PGE_2 agonist, a statin, an anti-DKK1 antibody or inhibitor, an anti-RANK ligand (RANKL) antibody (e.g., PROLIA®) or RANKL inhibitor, strontium ranelate, vitamin D, or a vitamin D derivative or mimic thereof. In some examples, the second bone-enhancing agent is Forteo® (Teriparatide, or recombinant human parathyroid hormone analog (1-34)) or Preotact® (parathyroid hormone). In some or any examples, the bone-enhancing agent is Protelos®.

[0020] In some examples, the second bone-enhancing agent is administered concurrently with the sclerostin inhibitor (e.g., for a length of time within the treatment period). In other examples, the second bone-enhancing agent is administered for a length of time once the treatment period with the sclerostin inhibitor has ended (i.e., for a maintenance period). In such examples, the second bone-enhancing agent is administered for a maintenance period of about 1 week to about 5 years.

[0021] The method may further comprise subsequently administering one or more amounts of a sclerostin inhibitor effective to maintain bone mineral density, optionally for a maintenance period of at least about 12 weeks, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years or longer (e.g., over the lifetime of the subject) after the treatment period has ended.

[0022] Periodontal disease treatment plans may also include supportive follow-up therapy after active treatment is completed. Supportive follow-up therapies include, but are not limited to mechanical debridement, reinforcement of oral hygiene (e.g., regular professional cleanings, daily brushing and flossing) and administration of antibiotics.

[0023] In any of the examples disclosed herein, the sclerostin inhibitor is optionally a sclerostin binding agent (e.g., an anti-sclerostin antibody or antibody fragment). The use of a sclerostin binding agent disclosed in U.S. Patent Publication No. 2007/0110747 in any of the methods disclosed herein or for preparation of medicaments for administration according to any of the methods disclosed herein is specifically contemplated. One or more doses of the sclerostin inhibitor are administered in an amount and for a time effective to treat alveolar bone loss. In various examples, one or more doses comprising from about 50 milligrams

to about 1,000 milligrams of sclerostin inhibitor are administered per week to a subject (e.g., a human subject). For example, a dose of sclerostin inhibitor (e.g., anti-sclerostin antibody or antibody fragment) can comprise at least about 5 mg, 15 mg, 25 mg, 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 120 mg, about 150 mg, about 200 mg, about 240 mg, about 250 mg, about 280 mg, about 300 mg, about 350 mg, about 400 mg, about 420 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg or up to about 1,000 mg of sclerostin inhibitor. Ranges between any and all of these endpoints are also contemplated, e.g. about 50 mg to about 80 mg, about 70 mg to about 140 mg, about 75 mg to about 100 mg, about 100 mg to about 150 mg, about 140 mg to about 210 mg, or about 150 mg to about 200 mg, or about 280 to about 410 mg. The dose is administered at any interval, such as multiple times a week (e.g., twice or three times per week), once a week, once every two weeks, once every three weeks, or once every four weeks. In some or any examples, a dose of sclerostin inhibitor (e.g., anti-sclerostin antibody or antibody fragment) ranging from about 120 mg to about 210 mg is administered twice a week. In some or any examples, a dose of about 140 mg of the sclerostin inhibitor (e.g., anti-sclerostin antibody or antibody fragment) is administered twice a week.

[0024] In some examples, the one or more doses of sclerostin inhibitor can comprise between about 0.1 to about 50 milligrams (e.g., between about 5 and about 50 milligrams), or about 1 to about 100 milligrams, of sclerostin inhibitor per kilogram of body weight (mg/kg). For example, the dose of sclerostin inhibitor (e.g., anti-sclerostin antibody or antibody fragment) may comprise at least about 0.1 mg/kg, 0.5 mg/kg, 1 mg/kg, about 2 mg/kg, about 3 mg/kg, about 4 mg/kg, about 5 mg/kg, about 6 mg/kg, about 7 mg/kg, about 8 mg/kg, about 9 mg/kg, about 10 mg/kg, about 20 mg/kg, about 25 mg/kg, about 26 mg/kg, about 27 mg/kg, about 28 mg/kg, about 29 mg/kg, about 30 mg/kg, about 31 mg/kg, about 32 mg/kg, about 33 mg/kg, about 34 mg/kg, about 35 mg/kg, about 36 mg/kg, about 37 mg/kg, about 38 mg/kg, about 39 mg/kg, about 40 mg/kg, about 41 mg/kg, about 42 mg/kg, about 43 mg/kg, about 44 mg/kg, about 45 mg/kg, about 46 mg/kg, about 47 mg/kg, about 48 mg/kg, or about 49 mg/kg, or about 50 mg/kg, about 55 mg/kg, about 60 mg/kg, about 65 mg/kg, about 70 mg/kg, about 75 mg/kg, about 80 mg/kg, about 85 mg/kg, about 90 mg/kg, about 95 mg/kg, or up to about 100 mg/kg. Ranges between any and all of these endpoints are also contemplated, e.g., about 1 mg/kg to about 3 mg/kg, about 1 mg/kg to about 5 mg/kg, about 1 mg/kg to about 10 mg/kg, about 1 mg/kg to about 20 mg/kg, about 1 mg/kg to about 40 mg/kg, about 5 mg/kg to about 30 mg/kg, or about 5 mg/kg to about 20 mg/kg.

[0025] Also described herein is the use of an effective amount of an anti-sclerostin inhibitor for treating alveolar bone loss in a subject, for example, in any of the amounts described above, such as from about 50 mg to about 1,000 mg per week, wherein one or more administrations of the sclerostin binding agent is carried out over a treatment period lasting at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 3 months, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 4 months, 17 weeks, 18 weeks 19 weeks, 20 weeks, 5 months, 21 weeks, 22 weeks, 23 weeks, 24 weeks, 6 months, 25 weeks, 26 weeks, 27 weeks, 28 weeks, 7 months, 29 weeks, 30 weeks, 31 weeks or longer (e.g., 8 months, 9 months, 10 months, 11 months, 1 year, 15 months, 18 months or longer).

[0026] In some or any examples, the sclerostin inhibitor is administered subcutaneously. In other examples, the sclerostin inhibitor is administered locally to the jaw of the subject. In some or any examples, the sclerostin inhibitor is administered locally to the diseased gingival area of the subject. In some or any examples, the sclerostin inhibitor is administered to the periodontal pocket of the subject.

[0027] The sclerostin inhibitor (e.g., anti-sclerostin antibody or antibody fragment) may be also used in the preparation of a medicament for administration to a subject with alveolar bone loss using any of the dosing and/or timing regimens described herein. Thus, the disclosure also contemplates sclerostin inhibitor for use according to any of the dosing and/or timing regimens described herein. Optionally, the sclerostin inhibitor is presented in a container, such as a single dose or multidose vial or syringe. The disclosure includes a container comprising anti-sclerostin antibody or fragment thereof and instructions for administering the antibody or fragment thereof for treating alveolar bone loss according to any of the dosing and/or timing regimens described herein.

[0028] In various examples, the sclerostin inhibitor is a sclerostin binding agent, e.g., an anti-sclerostin antibody or antibody fragment. Optionally, the anti-sclerostin antibody or antibody fragment 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 and/or 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.

[0029] In some examples, the anti-sclerostin antibody comprises a CDR-H1 of SEQ ID NO:245, a CDR-H2 of SEQ ID NO:246, a CDR-H3 of SEQ ID NO:247, a CDR-L1 of SEQ ID NO:78, a CDR-L2 of SEQ ID NO:79 and a CDR-L3 of SEQ ID NO:80.

[0030] In one example, the anti-sclerostin antibody comprises heavy chains comprising SEQ ID NO: 378 and light chains comprising SEQ ID NO: 376. In another example, anti-sclerostin antibody has heavy chains of SEQ ID NO: 145 or SEQ ID NO: 392 and light chains of SEQ ID NO: 141.

[0031] In another example, the anti-sclerostin antibody comprises CDRs of SEQ ID NOs: 20-25 of International Patent Publication No. WO 2008/115732 (SEQ ID NOs: 416-421), CDRs of SEQ ID NOs: 26-31 of International Patent Publication No. WO 2008/115732 (SEQ ID NOs: 422-427), CDRs of SEQ ID NOs: 32-37 of International Patent Publication No. WO 2008/115732 (SEQ ID NOs: 428-433), or CDRs of SEQ ID NOs: 4, 15, 26, 37, 48, and 59 of International Patent Publication No. WO 2009/047356 (SEQ ID NOs: 443, 454, 465, 476, 487, and 498, respectively). In yet another example, the anti-sclerostin antibody comprises an amino acid sequence of at least one of SEQ ID NOs: 135-143, 153-161, or 171-179 of International Patent Publication No. WO 2010/130830 (SEQ ID NOs: 745-753, 763-771, 781-789, respectively).

[0032] Also contemplated are dental implants, matrices, gels and wound dressings comprising an anti-sclerostin antibody (or antibody fragment) described herein. In some examples, the dental implants, matrices, gels and wound dressings are coated with an anti-sclerostin antibody (or antibody fragment). In other examples, the anti-sclerostin antibody (or antibody fragment) is formulated with a carrier described herein and applied to a target area (i.e., diseased gingival area or diseased periodontal pocket of the subject), optionally prior to (or after) application of a dental implant, matrices or wound dressing. The anti-sclerostin antibody (or antibody fragment) can be applied by any means known in the art. In some examples, the sclerostin antibody (or antibody fragment) is administered to a target area by subcutaneous injection prior to the application of the dental implant, matrix or wound dressing. In other examples, the sclerostin antibody (or antibody fragment) is administered to the affected area by brushing or otherwise coating the affected area prior to the application of the dental implant, matrix or wound dressing.

[0033] In addition, the use of an anti-sclerostin antibody (or antibody fragment) in any of the methods disclosed herein or for preparation of medicaments for administration according to any of the methods disclosed herein is specifically contemplated. In this regard, the

disclosure includes an anti-sclerostin antibody for use in a method of treating alveolar bone loss in a subject, the method comprising administering an anti-sclerostin antibody (or antibody fragment) in an amount effective to decrease the distance between the cement-enamel junction and the alveolar bone crest, optionally at a dose from about 5 mg to about 1,000 mg per week.

[0034] The disclosure also includes the use of an anti-sclerostin antibody (or antibody fragment) in preparation of a medicament for treating alveolar bone loss in a subject in an amount effective to decrease the distance between the cement-enamel junction and the alveolar bone crest, wherein the anti-sclerostin antibody (or antibody fragment) is optionally at a dose from about 5 mg to about 1,000 mg per week.

[0035] The foregoing summary is not intended to define every aspect of the invention, and additional aspects are described in other sections, such as the Detailed Description. The entire document is intended to be related as a unified disclosure, and it should be understood that all combinations of features described herein are contemplated, even if the combination of features are not found together in the same sentence, or paragraph, or section of this document. With respect to aspects of the invention described or claimed with "a" or "an," it should be understood that these terms mean "one or more" unless context unambiguously requires a more restricted meaning. The term "or" should be understood to encompass items in the alternative or together, unless context unambiguously requires otherwise. If aspects of the invention are described as "comprising" a feature, embodiments also are contemplated "consisting of" or "consisting essentially of" the feature.

BRIEF DESCRIPTION OF THE FIGURES

[0036] Figure 1 is a chart listing amino acid sequences and sequence identifiers for amino acid sequences of various anti-sclerostin antibodies described herein. The sequence identifiers refer to amino acid sequences provided in the Sequence Listing submitted herewith. The amino acid sequences also are set forth in U.S. Patent Publication No. 2007/0110747 or International Patent Publication Nos. WO 2008/115732, WO 2009/047356, or WO 2010/130830, hereby incorporated by reference.

[0037] Figures 2A and 2B are graphs depicting the effect of system administration (measured at the 2-week and 4-week study endpoints) of an anti-sclerostin antibody on bone volume fraction (Figure 2A) and bone mineral density (Figure 2B) during experimental periodontitis.

WHAT IS CLAIMED IS:

1. An anti-sclerostin antibody for use in treating alveolar bone loss by increasing alveolar bone height, wherein the anti-sclerostin antibody crossblocks or is crossblocked by an anti-sclerostin antibody that binds to a sub-region of SEQ ID NO: 1 comprising SEQ ID NO: 2 (DVSEYSCRELHFTR; corresponding to amino acids 51-64 of SEQ ID NO: 1), SEQ ID NO: 3 (SAKPVTELVCSGQCGPAR; corresponding to amino acids 73-90 of SEQ ID NO: 1), SEQ ID NO: 4 (WWRPSGPDFRCIPDRYR; corresponding to amino acids 101-117 of SEQ ID NO: 1) and SEQ ID NO: 5 (LVASCKCKRLTR; corresponding to amino acids 138-149 of SEQ ID NO: 1); wherein the anti-sclerostin antibody comprises

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

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

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

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

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

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

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

h) CDR sequences of SEQ ID NOs:242, 243, and 244 and CDR sequences of SEQ ID NOs:272, 273, and 274.

2. The antibody for use of claim 1, wherein the anti-sclerostin antibody is to be administered in an amount from about 120-270 mg.

3. The antibody for use of claim 1, wherein the anti-sclerostin antibody is to be administered twice a week.

4. The antibody for use of claim 1, wherein the anti-sclerostin antibody is to be administered locally to diseased gingival area or diseased periodontal pocket of the subject.

5. The antibody for use of any one of claims 1-4, wherein the treating further comprises that a standard of care therapeutic selected from the group consisting of doxycycline or chemically modified tetracycline-3 (CMT-3) is to be administered prior to administration of the anti-sclerostin antibody.

6. The antibody for use of any one of claims 1-5, wherein the treatment further comprises that a second bone-enhancing therapeutic is to be administered, selected from the group consisting of parathyroid hormone, teriparatide, a bisphosphonate, a Receptor Activator of Nuclear Kappa B Ligand (RANKL) antibody and a dickkopf (DKK-1) antibody.

7. The antibody for use of claim 6, wherein the second bone-enhancing therapeutic is to be administered after the treatment period with the anti-sclerostin antibody has ended.

8. The antibody for use of claim 1, wherein the anti-sclerostin antibody is to be administered for a second period of time in an amount sufficient to maintain alveolar bone.

9. The antibody for use of any one of claims 1-8, wherein the anti-sclerostin antibody is an immunoglobulin comprising a heavy chain and a light chain.

10. The antibody for use of any one of claims 1-9, wherein the anti-sclerostin antibody demonstrates a binding affinity for sclerostin of SEQ ID NO: 1 of less than or equal to 1×10^{-9} M.