CLAIMS

1. Use of a monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) and reduces human NOTUM activity in a trisodium 8-octanoyloxypyrene-1,3,6-trisulfonate (OPTS) assay *in vitro*, in the manufacture of a medicament for treating or preventing a disease or disorder characterized by bone loss in a patient.

2. The use according to claim 1, wherein the disease or disorder is selected from the group consisting of osteoporosis, osteopenia, and Paget's disease.

3. The use according to claim 2, wherein the osteoporosis is selected from the group consisting of postmenopausal osteoporosis, steroid- or glucocorticoid-induced osteoporosis, male osteoporosis and idiopathic osteoporosis.

4. The use according to any 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 use according to any of the preceding claims, wherein the antibody binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with KD of less than 50 nM, preferably less than 20 nM, or more preferably less than 10 nM.

6. The use according to any 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) 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;

f) 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;

g) 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;

h) 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;

i) 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.

7. The use according to any of the preceding claims, wherein the antibody is selected from a mouse antibody, a chimeric antibody, a humanized antibody, and a human antibody.

8. The use according to any of the preceding claims, 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: 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 wherein 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

b) 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

c) 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 wherein 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

d) 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

e) 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.

9. The use according to claim 8, wherein

a) in the antibody recited in claim 8, part (a): 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 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 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

b) in the antibody recited in claim 8, part (b): 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 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 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

c) in the antibody recited in claim 8, part (c): 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 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 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

d) in the antibody recited in claim 8, part (d): 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 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 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

e) in the antibody recited in claim 8, part (e): 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.

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

b) 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.

11. The monoclonal antibody according to claim 10, wherein

a) in the antibody of claim 10, part (a): 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 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 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

b) in the antibody of claim 10, part (b): the heavy chain variable region comprises an amino acid sequence of SEQ ID NO: 55 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 56.

12. A pharmaceutical composition comprising the antibody of either of claims 10 or 11.

13. A nucleic acid molecule comprising first and second polynucleotide sequences encoding the respective heavy and light chains of the antibody of either of claims 10 or 11.

14. A host cell comprising the nucleic acid molecule of claim 13.

15. A method of producing an antibody of either one of claims 10 or 11 comprising incubating the host cell of claim 14 under conditions sufficient to express the antibody.