Claims

1. A method of preparing an antibody suitable for use in a canine comprising the steps of:

- providing a donor antibody from a species other than a canine, wherein the donor antibody has binding specificity for a target antigen present in canines;

- comparing each amino acid residue of the amino acid sequence of framework regions of the donor antibody with each amino acid residue present at a corresponding position in the amino acid sequence of framework regions of one or more canine antibodies to identify one or more amino acid residues within the amino acid sequence of the framework regions of the donor antibody that differ from one or more amino acid residues at the corresponding position within the amino acid sequence of framework regions of the one or more canine antibodies; and

- substituting the one or more identified amino acid residues in the donor antibody with the one or more amino acid residues present at the corresponding position in the one or more canine antibodies.

2. The method as claimed in claim 1 wherein the step of substituting the one or more identified amino acid residues comprises substituting the one or more identified amino acid residues with the one or more amino acid residues present at the corresponding position which have the highest homology to the one or more substituted amino acid residues.

3. The method as claimed in claim 1 or 2 wherein the method further comprises the step of replacing constant domains of the heavy chain and/or light chain of the donor antibody with constant domains of a heavy and/or light chain from a canine antibody.

4. The method as claimed in claim 3 wherein the constant domain of the heavy chain is replaced with a type HCA or HCD canine constant domain.

5. The method as claimed in any one of claims 1 to 4 wherein the target antigen is nerve growth factor (NGF).

6. A neutralising antibody or an antigen binding fragment thereof which is capable of specifically binding to canine nerve growth factor (NGF) wherein the antibody or antibody binding fragment comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 or an amino acid sequence which has an identity of at least 85% thereto and/or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 or an amino acid sequence which has an identity of at least 85% thereto.

7. The antibody or antigen binding fragment thereof as claimed in claim 6 wherein the antibody is a chimeric or caninised antibody.

8. The antibody or antigen binding fragment thereof as claimed in claim 6 or claim 7 wherein the heavy chain constant domains of the antibody are selected or modified by way of amino acid substitution or deletion such that said constant domains do not mediate downstream effector functions.

9. The antibody or antigen binding fragment thereof as claimed in any one of claims 6 to 8 wherein the light chain comprises the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:10, or an amino acid sequence which has an identity of at least 85% thereto.

10. The antibody or antigen binding fragment thereof as claimed in any one of claims 6 to 9 wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, or an amino acid sequence which has a sequence identity of at least 85% thereto.

11. The antibody or antigen binding fragment thereof as claimed in any one of claims 6 to 9 wherein the heavy chain comprises the amino acid sequence selected from the group consisting of SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22, or an amino acid sequence which has a sequence identity of at least 85% thereto.

12. The antibody or antigen binding fragment thereof as claimed in any one of claims 6 to 9 wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:18, SEQ ID NO:19, and SEQ ID NO:22, or an amino acid sequence which has a sequence identity of at least 85% thereto.

13. An anti-canine NGF antibody, or canine NGF binding fragment thereof, comprising a light chain variable region comprising at least one of:

an FR1 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:23 or SEQ ID NO:24,

an FR2 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:25,

an FR3 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:26 or SEQ ID NO:27,

an FR4 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:28,

and/or a heavy chain variable region comprising at least one of:

an FR1 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:29,

an FR2 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:30,

an FR3 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:31 or SEQ ID NO:32,

an FR4 framework region consisting or comprising of the amino acid sequence of SEQ ID NO:33.

14. The anti-canine NGF antibody or canine NGF binding fragment as claimed in claim 13 which comprises a light chain variable domain having an FR1 region of SEQ ID NO:23 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: amino acid residue Q3 is V, T5 is M, S7 is T, A9 is L, L13 is V, Q15 is P or R, E16 is G, K18 is T or P, V19 is A, T20 is S, T22 is S, T5 is I, A9 is P, S12 is A, S14 is R or T, E16 is D, E17 is D, K18 is A, E or L, T22 is Y and C23 is Y.

15. The anti-canine NGF antibody or canine NGF binding fragment as claimed in claim 13 which comprises a light chain variable domain having the FR1 region of SEQ ID NO:24 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: residue V3 is Q, T5 is M, S7 is T, A9 is L, L13 is V, Q15 is P or R, E16 is G, K18 is T or P, V19 is A, T20 is S, T22 is S, T5 is I, A9 is P, S12 is A, S14 is R or T, E16 is D, E17 is D, K18 is A, E or L, T22 is Y and C23 is Y.

16. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 15 which comprises a light chain variable domain having the FR2 region of SEQ ID NO:25 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: Y2 is F, Q3 is R, A9 is S, K11 is Q, L12 is R, Y2 is I or L, Q3 is I or L, Q4 is H, K5 is R, P6 is A or S, G7 is D, A9 is P or T, K11 is E or R, L12 is A, G, P or S, I14 is L, and Y15 is E, F, N, S or V.

17. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 16 which comprises a light chain variable domain having the FR3 region of SEQ ID NO:26 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: S4 is D, E14 is D, Y15 is F, S16 is T, L17 is F, T18 is K, N20 is S, L22 is V, S24 is P, V27 is A, F31 is

Y, G1 is A, V2 is A, P3 is S, F6 is L or V, S7 is I, G8 is A, T13 is A, S16 is R, T18 is R, S24 is A, E25 is D, G, I or N, V27 is G, S or T, A28 is G, and V29 is I or L.

18. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 16 which comprises a light chain variable domain having the FR3 region of SEQ ID NO:27 has been modified by one or more of the amino acid substitutions selected from the group consisting of: S4 is D, E14 is D, F15 is Y, S16 is T, L17 is F, T18 is K, S20 is N, L22 is V, P24 is S, V27 is A, Y31 is F, G1 is A, V2 is A, P3 is S, F6 is L or V, S7 is I, G8 is A, T13 is A, S16 is R, T18 is R, S24 is A, E25 is D, G, I or N, V27 is G, S or T, A28 is G, and V29 is I or L.

19 The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 18 which comprises a light chain variable domain having the FR4 region of SEQ ID NO:28 has been modified by one or more of the amino acid substitutions selected from the group consisting of: E8 is D, G2 is S, A3 is P, Q or T, G4 is E, T5 is P, K6 is Q or S, V7 is L or W, E8 is R, or L9 is I.

20. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 19 which comprises a heavy chain variable domain having the FR1 region of SEQ ID NO:29 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: D10 is G, N13 is Q, G15 is T, G16 is E, T17 is S, T19 is R, V24 is A, S28 is T, L29 is F, T30 is S, E1 is D or G, V2 is E, G,I, L or M, Q3 is A, E, H, K, L, P, R, S or V, L4 is P or V, V5 is A, E, L or M, E6 is A or Q, S7 is F, L or T, G9 is E, D10 is A, E, N or T, L11 is Q, R, V or W, V12 is A, I or M, N13 is K or R, P14 is F or T, G15 is A or E, G16 is A, T17 is P, L18 is R, T19 is G, K or V, L20 is I or V, S21 is Y, V23 is A, E, I or L, V24 is G, I, S or T, S25 is G, P or T, G26 is D, R or T, F27 is D, I, L, S, T or V, S28 is A, D, I, L, M, N, P or R, L29 is I, M or V, T30 is D, G, H, I, K, N, R, V.

21. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 20 which comprises a heavy chain variable domain having the FR2 region of SEQ ID NO:30 which has been modified by one or more

of the amino acid substitutions selected from the group consisting of: L6 is P, R8 is K, E11 is Q, G14 is A, W1 is C, V2 is A, F, I or L, Q4 is H or L, A5 is D, G, P, S, T or V, G7 is E, L or R, R8 is A, E, G, M or Q, G9 is D, E, R, T or V, L10 is F, M or P, E11 is D, H, L, P or R, W12 is C, F, L, M, S or Y, V13 is F, I or L, G14 is L,S or T.

22. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 21 which comprises a heavy chain variable domain having the FR3 region of SEQ ID NO:31 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: L2 is F, T5 is S, T8 is N, S9 is A, S11 is N, V13 is L, F14 is Y, K16 is Q, H18 is N, Q21 is R, S22 is A, T27 is V, R32 is K, R1 is Q, L2 is V, T3 is A, I or S, I4 is L, M, T or V, T5 is A or F, R6 is K, D7 is E or N, T8 is D, G, I or S, S9 is D, G, P, T or V, K10 is E, G, M, N, Q or R, S11 is D, H, K or R, T12 is A, I, M or S, V13 is A, I or M, F14 is H, S or T, L15 is I, K16 is A, D, E, H or R, M17 is L, H18 is D, K, P, R, S or T, S19 is D, G, N, R or T, L20 is V, Q21 is G, I, K, S or T, S22 is D, G, P, T or V, E23 is A, D or V, T25 is A, M or S, A26 is G or V, T27 is F, I, K, L, M or Q, Y28 is H, Y29 is F or H, A31 is C, G, L, M, R, S, T or V, R32 is A, D, E, G, I, L, M, N, P, Q, S, T or V.

23. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 21 which comprises a heavy chain variable domain having the FR3 region of SEQ ID NO:32 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: L2 is F, T5 is S, T8 is N, S9 is A, S11 is N, V13 is L, F14 is Y, Q16 is K, H18 is N, R21 is Q, S22 is A, T27 is V, R32 is K, R1 is Q, L2 is V, T3 is A, I or S, I4 is L, M, T or V, T5 is A or F, R6 is K, D7 is E or N, T8 is D, G, I or S, S9 is D, G, P, T or V, K10 is E, G, M, N, Q or R, S11 is D, H, K or R, T12 is A, I, M or S, V13 is A, I or M, F14 is H, S or T, L15 is I, K16 is A, D, E, H or R, M17 is L, H18 is D, K, P, R, S or T, S19 is D, G, N, R or T, L20 is V, Q21 is G, I, K, S or T, S22 is D, G, P, T or V, E23 is A, D or V, T25 is A, M or S, A26 is G or V, T27 is F, I, K, L, M or Q, Y28 is H, Y29 is F or H, A31 is C, G, L, M, R, S, T or V, R32 is A, D, E, G, I, L, M, N, P, Q, S, T or V.

24. The anti-canine NGF antibody or canine NGF binding fragment as claimed in any one of claims 13 to 23 which comprises a heavy chain variable domain having the FR4 region of SEQ ID NO:33 which has been modified by one or more of the amino acid substitutions selected from the group consisting of: W1 is L, G2 is A or S, Q3 is D, H, P or R, T5 is A, I, N or S, L6 is P, Q or R, V7 is I, L or P, T8 is A, F, I, L, P, S or Y, V9 is A, S10 is A, C, P or T, S11 is A, L or P.

25. The antibody as claimed in any one of claims 13 to 24 wherein the antibody has a type HCA or HCD canine constant domain.

26. An antibody prepared according to the method of any one of claims 1 to 5, or a binding fragment thereof.

27. The antibody or antigen binding fragment thereof as claimed in any one of claims 6 to 26 wherein binding of the antibody or fragment to canine NGF inhibits the ability of canine NGF to bind to the p75 or the TrkA canine NGF receptors.

28. The antibody or binding fragment as claimed in any one of claims 6 to 27 which specifically binds to canine NGF with a binding affinity having an equilibrium dissociation constant (K_D) of $1X10^{-8}$ or less.

29. The antibody or binding fragment as claimed in any one of claims 6 to 28 wherein the antigen binding fragment is selected from the group consisting of a single chain Fv (scFv) antibody fragment, a Fab antibody fragment, a Fab' antibody fragment and a $F(ab')_2$ antibody fragment.

30. The antibody or binding fragment as claimed in any one of claims 6 to 29 wherein the antibody is a multispecific or multivalent antibody.

31. The antibody or binding fragment as claimed in any one of claims 6 to 30 wherein the antibody or binding fragment has a serum life in canines of at least one week.

32. The antibody or binding fragment as claimed in any one of claims 6 to 31 wherein the antibody or binding fragment is not immunogenic in canines.

33. The antibody or binding fragment as claimed in any one of claims 6 to 32 wherein the antibody is purifiable by a method comprising the steps of anion exchange chromatography, hydrophobic interaction chromatography and size exclusion chromatography.

34. The antibody or binding fragment as claimed in any one of claims 6 to 33 wherein the antibody is purifiable by a method comprising the steps of Captoadhere affinity chromatography and anion exchange chromatography.

35. A method for treating, inhibiting or ameliorating pain in a canine, the method comprising the steps of:

- providing a therapeutically effective amount of an anti-canine NGF antibody, or antigen binding fragment thereof, wherein the antibody is a caninised antibody,and
- administering the same to a canine in need thereof.

36. The method as claimed in claim 35 wherein the anti-canine NGF antibody is an antibody as claimed in any one of claims 6 to 34 or an antigen binding fragment thereof.

37. The method as claimed in claim 35 wherein the anti-canine NGF antibody comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 or a sequence which has at least 85% identity thereto and/or a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 or an amino acid sequence having at least 85% sequence homology thereto.

38. The method as claimed in claim 35 wherein the anti-canine NGF antibody comprises a light chain having the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:10 or a sequence having a sequence identity of at least 85% thereto and/or a heavy chain which comprises, consists of or consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, or an amino acid sequence having a sequence identity of at least 85% thereto.

39. The method as claimed in any one of claims 35 to 38 wherein the pain is selected from the group consisting of neuropathic pain, inflammatory pain, pruritic pain, peri-operative, post-operative and post-surgical pain.

40. The method as claimed in claim 39 wherein the post operative pain is selected from the group consisting of orthopaedic surgery, soft tissue surgery, ovariohysterectomy procedures and castration procedures.

41. A method for the treatment of arthritis or an arthritic condition in a canine subject, said method comprising the steps of:

- providing a therapeutically effective amount of an anti-canine NGF antibody, or antigen binding fragment thereof, wherein the antibody is a caninised antibody, and
- administering the same to a canine in need thereof.

42. The method as claimed in claim 41 wherein the anti-canine NGF antibody is an antibody as claimed in any one of claims 6 to 34.

43. The method as claimed in claim 41 wherein the anti-canine NGF antibody comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 or a sequence which has at least 85% identity thereto and/or a heavy chain variable domain comprising the amino acid sequence

of SEQ ID NO:2 or SEQ ID NO:4 or an amino acid sequence having at least 85% sequence homology thereto.

44. The method as claimed in claim 41 wherein the anti-canine NGF antibody comprises a light chain having the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:10 or a sequence having a sequence identity of at least 85% thereto and/or a heavy chain which comprises, consists of or consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, or an amino acid sequence having a sequence identity of at least 85% identity thereto.

45. The method as claimed in any one of claims 41 to 44 wherein the arthritis or arthritic condition includes the conditions selected from the group consisting of immune mediated polyarthritis, rheumatoid arthritis and osteoarthritis.

46. The method as claimed in any one of claims 41 to 45 wherein the treatment of the arthritis or arthritic condition comprises ameliorating, inhibiting, reducing, suppressing or delaying the onset of pain associated with, or attributable to, the arthritic condition.

47. A method for the treatment of a condition caused by, associated with or resulting in the increased expression of canine NGF or increased sensitivity to NGF in a canine subject, said method comprising the steps of:

- providing a therapeutically effective amount of an anti-canine NGF antibody, or antigen binding fragment thereof, wherein the antibody is a caninised antibody, and
- administering the same to a canine in need thereof.

48. The method as claimed in claim 47 wherein the anti-canine NGF antibody is an antibody as claimed in any one of claims 6 to 34.

49. The method as claimed in claim 47 wherein the anti-canine NGF antibody comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 or a sequence which has at least 85% identity thereto and/or a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 or an amino acid sequence having at least 85% sequence homology thereto.

50. The method as claimed in claim 47 wherein the anti-canine NGF antibody comprises a light chain having the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:10 or a sequence having a sequence identity of at least 85% thereto and/or a heavy chain which comprises, consists of or consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, or an amino acid sequence having a sequence identity of at least 85% identity thereto.

51. A method for the treatment of a tumour induced to proliferate by NGF in a canine and conditions associated therewith, said method comprising the steps of:

- providing a therapeutically effective amount of an anti-canine NGF antibody, or antigen binding fragment thereof, wherein the antibody is a caninised antibody, and
- administering the same to a canine in need thereof.

52. The method as claimed in claim 51 wherein the anti-canine NGF antibody is an antibody as claimed in any one of claims 6 to 34.

53. The method as claimed in claim 51 wherein the anti-canine NGF antibody comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 or a sequence which has at least 85% identity thereto and/or a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 or an amino acid sequence having at least 85% sequence homology thereto.

54. The method as claimed in claim 51 wherein the anti-canine NGF antibody comprises a light chain having the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:10 or a sequence having a sequence identity of at least 85% thereto and/or a heavy chain which comprises, consists of or consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, or an amino acid sequence having a sequence identity of at least 85% identity thereto.

55. The method as claimed in any one of claims 51 to 54 wherein the tumour is induced to proliferate by autocrine or paracrine NGF.

56. The method as claimed in claim 55 wherein the tumour is an osteosarcoma.

57. The method of any one of claims 35 to 56 further comprising the step of co-administering at least one further therapeutic agent.

58. The method as claimed in claim 57 wherein the at least one therapeutic agent is selected from the group consisting of an analgesic, an NSAID, an opioid, a corticosteroid and a steroid.

59. The method as claimed in claim 57 wherein the at least one therapeutic agent is selected from the group consisting of an antibiotic, an antifungal therapeutic agent, an antiprotozoal therapeutic agent and an antiviral therapeutic agent.

60. The method as claimed in claim 57 wherein the at least one therapeutic agent is selected from the group consisting of an inhibitor of a mediator of inflammation, a PGE-receptor antagonist, an immunosuppressive agent, cyclosporine, an anti-inflammatory glucocorticoid, an agent for use in the treatment of cognitive dysfunction or cognitive impairment, an anti-hypertensive, a

compound used for the treatment of cardiovascular dysfunction, a diuretic, a vasodilator, a beta-adrenergic receptor antagonist, an angiotensin-II converting enzyme inhibitor, a calcium channel blocker and a HMG-CoA reductase inhibitor.

61. The method of any one of claims 35 to 60 wherein the antibody or antigen binding fragment is administered to a canine at a dose ranging from about 0.01 mg/kg of body weight to about 10 mg/kg of body weight.

62. The method of any one of claims 35 to 60 wherein the antibody or antigen binding fragment is administered to a canine at a dose ranging from about 0.03 mg/kg of body weight to about 3 mg/kg of body weight.

63. A pharmaceutical composition for treating pain or a condition resulting in or caused by pain in a canine or a tumour induced to proliferate by NGF, comprising a therapeutically effective amount of an anti-canine NGF caninised antibody or binding fragment thereof according to any one of claims 6 to 34 along with at least one pharmaceutically acceptable carrier, excipient or diluent.

64. The pharmaceutical composition as claimed in claim 63 further comprising at least one analgesic, NSAID, opioid, corticosteroid or steroid.

65. The pharmaceutical composition as claimed in claim 63 or 64 wherein the condition resulting in pain is selected from the group consisting of rheumatoid arthritis, osteoarthritis, pruritis, inflammation, immune mediated polyarthritis, acute pain, chronic pain, surgical pain and post-surgical pain or the tumour induced to proliferate by NGF is an osteosarcoma.

66. An isolated nucleic acid that encodes an antibody or antigen binding fragment according to any one of claims 6 to 34.

67. An isolated nucleic acid which encodes the light chain variable domain of an anti-canine NGF caninised antibody or antibody fragment having the amino

acid sequence of SEQ ID NO:1 or SEQ ID NO:3, or a light chain having the amino acid sequence of SEQ ID NO:5 or 10.

68. An isolated nucleic acid which encodes the heavy chain variable domain of an anti-canine NGF caninised antibody or antibody fragment having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 or a heavy chain having the amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22.

69. The isolated nucleic acid as claimed in any one of claims 66 to 68 which is operably linked to one or more regulatory sequences.

70. An expression vector comprising a nucleic acid as claimed in any one of claims 66 to 69.

71. The expression vector as claimed in claim 70 further comprising one or more regulatory sequences.

72. The expression vector as claimed in claim 70 or 71 wherein the expression vector is a plasmid or a retroviral vector.

73. A host cell incorporating the expression vector as claimed in any one of claims 70 to 72.

74. A method for producing a caninised anti-canine NGF neutralising antibody, the method comprising the step of culturing a host cell as claimed in claim 73 to allow the cell to express a caninised anti-canine NGF neutralising antibody.

75. A method for treating, ameliorating or inhibiting pain or a tumour induced to proliferate by NGF in a canine, the method comprising the step of administering to

the canine a therapeutically effective amount of a nucleic acid according to any one of claims 66 to 69.

76. An antibody or antibody binding fragment according to any one of claims 6 to 34, a pharmaceutical composition according to any one of claims 63 to 65, a nucleic acid as claimed in any one of claims 66 to 69, or an expression vector as claimed in claims 70 to 72 for use in the treatment or prevention of pain in a canine.

77. The antibody or antibody binding fragment as claimed in claim 76 wherein the pain is selected from the group consisting of acute pain, chronic pain, peri-operative pain, post-operative pain, pain resulting orthopaedic surgery, pain associated with soft tissue surgery, pain resulting from ovariohysterectomy procedures, pain resulting from castration procedures, inflammatory pain, pruritic pain, chronic pain associated with cancer or a cancerous condition and pain associated with or resulting from rheumatoid arthritis or osteoarthritis.

78. An antibody or antibody binding fragment according to any one of claims 6 to 34, a pharmaceutical composition according to any one of claims 63 to 65, a nucleic acid as claimed in any one of claims 66 to 69, or an expression vector as claimed in claims 70 to 72 for use in the treatment of arthritis.

79. The antibody or antibody binding fragment as claimed in claim 78 wherein the arthritis is osteoarthritis, immune mediated polyarthritis or rheumatoid arthritis.

80. An antibody or antibody binding fragment according to any one of claims 6 to 34, a pharmaceutical composition according to any one of claims 63 to 65, a nucleic acid as claimed in any one of claims 66 to 69, or an expression vector as claimed in claims 70 to 72 for use in the treatment or prevention of a tumour induced to proliferate by NGF in a canine subject and conditions associated therewith.

81. The antibody or antibody binding fragment as claimed in claim 80 wherein the tumour is an osteosarcoma.

82. Use of an antibody or antibody binding fragment according to any one of claims 6 to 34, a pharmaceutical composition according to any one of claims 63 to 65, a nucleic acid as claimed in any one of claims 66 to 69, or an expression vector as claimed in claims 70 to 72 in the preparation of a medicament for the treatment or prevention of pain in a canine.

83. Use as claimed in claim 82 wherein the pain is selected from the group consisting of acute pain, chronic pain, peri-operative pain, post-operative pain, pain resulting orthopaedic surgery, pain associated with soft tissue surgery, pain resulting from ovariohysterectomy procedures, pain resulting from castration procedures, chronic pain associated with cancer or a cancerous condition and pain associated with or resulting from rheumatoid arthritis, inflammatory pain, pruritic pain, immune mediated polyarthritis or osteoarthritis.

84. Use of an antibody or antibody binding fragment according to any one of claims 6 to 34, a pharmaceutical composition according to any one of claims claims 63 to 65, a nucleic acid as claimed in any one of claims 66 to 69, or an expression vector as claimed in claims 70 to 72 in the preparation of a medicament for the treatment, inhibition amelioration or prevention of arthritis in a canine.

85. Use as claimed in claim 84 wherein the arthritis is osteoarthritis, immune mediated polyarthritis or rheumatoid arthritis.

86. Use of an antibody or antibody binding fragment according to any one of claims 6 to 34, a pharmaceutical composition according to any one of claims claims 63 to 65, a nucleic acid as claimed in any one of claims 66 to 69, or an expression vector as claimed in claims 70 to 72 in the preparation of a

medicament for the treatment of a tumour induced to proliferate by NGF in a canine and conditions associated therewith.

87. Use as claimed in claim 86 wherein the tumour is an osteosarcoma.

88. A cell line, or a derivative or progeny cell thereof that produces anti-canine NGF neutralising monoclonal antibodies, or fragments thereof according to any one of claims 6 to 34.

89. A kit for the treatment of pain in canines, or for the treatment of a condition associated with pain, or for the treatment, amelioration or inhibition of pain associated with immune mediated polyarthritis, osteoarthritis or rheumatoid arthritis, or for the treatment of a tumour induced to proliferate by NGF in a canine and conditions associated therewith, comprising an anti-canine NGF antibody or binding fragment according to any one of claims 6 to 34 and instructions for use of the same.

90. A diagnostic kit comprising an anti-canine NGF antibody or binding fragment according to any one of claims 6 to 34 for use in the detection of the anti-canine NGF monoclonal antibody or binding fragment.

CLAIMS

1. A method of preparing an antibody suitable for use in a canine comprising the steps of:

- providing a donor antibody from a species other than a canine, wherein the donor antibody has binding specificity for a target antigen present in canines;

- comparing each amino acid residue of the amino acid sequence of framework regions of the donor antibody with each amino acid residue present at a corresponding position in the amino acid sequence of framework regions of one or more canine antibodies to identify one or more amino acid residues within the amino acid sequence of the framework regions of the donor antibody that differ from one or more amino acid residues at the corresponding position within the amino acid sequence of framework regions of the one or more canine antibodies; and

- substituting the one or more identified amino acid residues in the donor antibody with the one or more amino acid residues present at the corresponding position in the one or more canine antibodies to produce a modified antibody,

wherein the modified antibody does not contain any amino acid in any position within the framework regions which would be foreign at the position in canines; and

wherein the modified antibody is capable of specifically binding to canine nerve growth factor (NGF) and inhibiting the ability of canine NGF to bind to the p75 or the TrkA canine NGF receptor.

2. An antibody or an antigen binding fragment thereof which is capable of specifically binding to canine nerve growth factor (NGF) and inhibiting the ability of canine NGF to bind to the p75 or the TrkA canine NGF receptor, wherein the antibody or antigen binding fragment comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:1 or an amino acid sequence which has an identity of at least 85% thereto and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:2 or an amino acid sequence which has an identity of at least 85% thereto, wherein the antibody or antigen

binding fragment thereof does not contain any amino acid in any position within the framework regions which would be foreign at the position in canines.

3. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the antibody or antigen binding fragment comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:2.

4. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the antibody or antigen binding fragment comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:3 and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:4.

5. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the antibody or antigen binding fragment comprises:

a light chain variable region comprising the amino acid sequence of SEQ ID NO:3 and further comprising the amino acid substitutions E16G, K18T, E70D and A100Q, and

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:4 and further comprising the amino acid substitutions D10G, N13Q, T17S, T19R, V24A, L41P, R43K, L67F, T70S, T73N, S74A, S76N, T92V and L117S.

6. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the light chain comprises the amino acid sequence of SEQ ID NO:5, or an amino acid sequence which has an identity of at least 85% thereto.

7. The antibody or antigen binding fragment thereof as claimed in claim 6, wherein the light chain comprises the amino acid sequence of SEQ ID NO:5.

8. The antibody or antigen binding fragment thereof as claimed in claim 6, wherein the light chain comprises the amino acid sequence of SEQ ID NO:10.

9. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 and SEQ ID NO:9, or an amino acid sequence which has a sequence identity of at least 85% thereto.

10. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, or an amino acid sequence which has a sequence identity of at least 85% thereto.

11. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the heavy chain comprises the amino acid sequence selected from the group consisting of SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17 and SEQ ID NO:18, or an amino acid sequence which has a sequence identity of at least 85% thereto.

12. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the heavy chain comprises the amino acid sequence selected from the group consisting of SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 and SEQ ID NO:22, or an amino acid sequence which has a sequence identity of at least 85% thereto.

13. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:15 and SEQ ID NO:18, or an amino acid sequence which has a sequence identity of at least 85% thereto.

14. The antibody or antigen binding fragment thereof as claimed in claim 2, wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NO:11, SEQ ID NO:14, SEQ ID NO:19 and SEQ ID NO:22, or an amino acid sequence which has a sequence identity of at least 85% thereto.

15. An antibody or binding fragment thereof which is capable of specifically binding to canine nerve growth factor (NGF) and inhibiting the ability of canine NGF

to bind to the p75 or the TrkA canine NGF receptor, wherein the antibody or binding fragment thereof comprises a light chain variable region and a heavy chain variable region, wherein the light chain variable region comprises:

an FR1 framework region comprising the amino acid sequence of SEQ ID NO:23 or an amino acid sequence which has a sequence identity of at least 85% thereto,

an FR2 framework region comprising the amino acid sequence of SEQ ID NO:25 or an amino acid sequence which has a sequence identity of at least 85% thereto,

an FR3 framework region comprising the amino acid sequence of SEQ ID NO:27 or an amino acid sequence which has a sequence identity of at least 85% thereto,

an FR4 framework region comprising the amino acid sequence of SEQ ID NO:28 or an amino acid sequence which has a sequence identity of at least 85% thereto,

and wherein the heavy chain variable region comprises:

an FR1 framework region comprising the amino acid sequence of SEQ ID NO:29 or an amino acid sequence which has a sequence identity of at least 85% thereto,

an FR2 framework region comprising the amino acid sequence of SEQ ID NO:30 or an amino acid sequence which has a sequence identity of at least 85% thereto,

an FR3 framework region comprising the amino acid sequence of SEQ ID NO:32 or an amino acid sequence which has a sequence identity of at least 85% thereto,

an FR4 framework region comprising the amino acid sequence of SEQ ID NO:33 or an amino acid sequence which has a sequence identity of at least 85% thereto;

and wherein the antibody or binding fragment thereof does not contain any amino acid in any position within the framework regions which would be foreign at the position in canines.

16. The antibody or binding fragment thereof as claimed in claim 15, wherein the light chain variable region comprises:

an FR1 framework region comprising the amino acid sequence of SEQ ID NO:23 or SEQ ID NO:24,

an FR2 framework region comprising the amino acid sequence of SEQ ID NO:25,

an FR3 framework region comprising the amino acid sequence of SEQ ID NO:26 or SEQ ID NO:27,

an FR4 framework region comprising the amino acid sequence of SEQ ID NO:28,

and wherein the heavy chain variable region comprises:

an FR1 framework region comprising the amino acid sequence of SEQ ID NO:29,

an FR2 framework region comprising the amino acid sequence of SEQ ID NO:30,

an FR3 framework region comprising the amino acid sequence of SEQ ID NO:31 or SEQ ID NO:32, and

an FR4 framework region comprising the amino acid sequence of SEQ ID NO:33.

17. The antibody or binding fragment thereof as claimed in claim 15, wherein the light chain variable region comprises:

an FR1 framework region comprising the amino acid sequence of SEQ ID NO:24 and further comprising the amino acid substitutions E16G and K18T,

an FR2 framework region comprising the amino acid sequence of SEQ ID NO:25,

an FR3 framework region comprising the amino acid sequence of SEQ ID NO:26 or SEQ ID NO:27 and further comprising the amino acid substitution E14D,

an FR4 framework region comprising the amino acid sequence of SEQ ID NO:28 and further comprising the amino acid substitution A3Q,

and wherein the heavy chain variable region comprises:

an FR1 framework region comprising the amino acid sequence of SEQ ID NO:29 and further comprising the amino acid substitutions D10G, N13Q, T17S, T19R and V24A,
an FR2 framework region comprising the amino acid sequence of SEQ ID NO:30 and further comprising the amino acid substitutions L6P and R8K,
an FR3 framework region comprising the amino acid sequence of SEQ ID NO:31 or SEQ ID NO:32 and further comprising the amino acid substitutions L2F, T5S, T8N, S9A, S11N and T27V, and
an FR4 framework region comprising the amino acid sequence of SEQ ID NO:33 and further comprising the amino acid substitution L6S.

18. The antibody or antigen binding fragment thereof as claimed in claim 2 or claim 15, comprising a heavy chain constant domain selected or modified by way of amino acid substitution or deletion such that said constant domain does not mediate downstream effector functions.

19. The antibody or antigen binding fragment thereof as claimed in claim 18 comprising an aglycosylated type HCB, HCA or HCD canine heavy chain constant domain.

20. The antibody or antigen binding fragment thereof as claimed in claim 18 comprising a type HCA or HCD canine heavy chain constant domain.

21. A pharmaceutical composition comprising the antibody or antigen binding fragment thereof as claimed in any one of claims 2 to 20 together with at least one pharmaceutically acceptable carrier, excipient or diluent.

22. The antibody or antigen binding fragment thereof as claimed in any one of claims 2 to 20 for use in the treatment of a condition associated with pain, or for the treatment, amelioration or inhibition of pain associated with immune mediated polyarthritis, osteoarthritis or rheumatoid arthritis, or for the treatment of a tumour

induced to proliferate by Nerve Growth Factor in a canine and conditions associated therewith.

23. A kit for the treatment of pain in canines, or for the treatment of a condition associated with pain, or for the treatment, amelioration or inhibition of pain associated with immune mediated polyarthritis, osteoarthritis or rheumatoid arthritis, or for the treatment of a tumour induced to proliferate by NGF in a canine and conditions associated therewith, comprising the antibody or antigen binding fragment thereof as claimed in any one of claims 2 to 20 and instructions for use of the same.