CLAIMS:

1. Use of an anti-IL-1β binding antibody or binding fragment thereof in the manufacture of a medicament for use in reducing a cardiovascular event in a subject, wherein the subject is a subject with a history of a previous cardiovascular event, wherein the cardiovascular event to be reduced is acute coronary syndrome, and wherein the previous cardiovascular event is myocardial infarction.

2. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in claim 1, wherein said subject also has a history of at least one risk factor for cardiovascular disease, wherein the risk factor is manifest coronary heart disease, coronary artery disease, thrombosis, transient ischaemic attack, left ventricular hypertrophy, arteriosclerosis, restenosis, tobacco smoking or peripheral vascular disease, or wherein the risk factor is elevated triglycerides, systemic inflammation, high blood phosphorus levels, high parathyroid hormone levels, microalbuminuria, or high homocysteine levels, or wherein the risk factor is obesity, hyperglycemia, chronic renal failure, high blood glucose, chronic kidney disease, or metabolic syndrome, or wherein the risk factor is hypertension, dyslipidemia, hyperlipidemia, elevated total cholesterol, elevated LDL cholesterol, or low HDL cholesterol or atherosclerosis.

3. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in claim 1, wherein the subject has elevated levels of C-reactive protein (CRP), wherein the subject is older than 55 years, wherein the subject is non-hypertensive, wherein the subject has diabetes mellitus, or wherein the subject has a history of two or more said risk factors.

4. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in claim 1, further comprising administering at least one other pharmaceutical composition comprising an active agent other than an anti-IL-1β binding antibody or binding fragment thereof.

5. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in claim 4, wherein the active agent of said at least one other pharmaceutical composition is a cholesterol lowering agent, a statin, an HMG-CoA reductase inhibitor, a calcium channel blocker, a beta blocker, an antihypertensive, a diuretic, aspirin, niacin, an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin II receptor blocker, a vasodilator, an anticoagulant, an inhibitor of platelet aggregation, a thrombolytic or digitalis.

6. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in claim 1, wherein said therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof is sufficient to achieve a decrease in CRP levels.

7. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to human IL-1β with a dissociation constant of about 500 pM or less.

8. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof is a neutralizing antibody.

9. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to an IL-1β epitope such that the bound antibody or fragment substantially permits the binding of IL-1β to IL-1 receptor I (IL-1RI).

10. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof competes with the binding of an antibody having the light chain variable region of SEQ ID NO:1 and the heavy chain variable region of SEQ ID NO:2

11. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to an epitope incorporating Glu64 of IL-1β.

12. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to amino acids 1-34 of the N terminus of IL-1β.

13. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof is to be administered in one or more doses of 1 mg/kg or less of antibody or fragment, wherein the one or more doses are at least 0.01 mg/kg of antibody or fragment.

14. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof is to be administered in one or more doses of 0.03 mg/kg to 1 mg/kg.

15. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-3, wherein the anti-IL-1β binding antibody or binding fragment thereof is to be administered as a fixed dose, independent of a dose per subject weight ratio.

16. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in claim 6, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 100 mg or less of antibody or fragment, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of at least 0.5 mg of antibody or fragment.

17. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-16, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered by subcutaneous, intravenous or intramuscular injection.

18. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in any one of claims 1-17, wherein administration of an initial dose of anti-IL-1β binding antibody or binding fragment thereof is followed by the administration of one or more subsequent doses.

19. The use of an anti-IL-1β binding antibody or binding fragment thereof as claimed in claim 18, wherein said initial dose and one or more subsequent doses are administered at an interval of about once every week to about once every 12 months.

CLAIMS:

1. A method of reducing a cardiovascular event in a subject, comprising administering to said subject a therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof, wherein the subject is a subject with a history of a previous cardiovascular event or a history of at least one risk factor for cardiovascular disease, and wherein the cardiovascular event is myocardial infarction, stroke, cardiovascular death, congestive heart failure, cardiac arrest, acute coronary syndrome, angina, or a revascularization procedure.

2. The method of claim 1, wherein the subject is a subject with a history of a previous cardiovascular event, and wherein the cardiovascular event is myocardial infarction, stroke, acute coronary syndrome, angina or a revascularization procedure.

3. The method of claim 1 or 2, wherein the revascularization procedure is a coronary, carotid or peripheral arterial revascularization procedure.

4. The method of claim 3, wherein the coronary, carotid or peripheral arterial revascularization procedure is a percutaneous coronary intervention (PCI), a stent implant, coronary artery bypass graft (CABG), carotid endarterectomy, peripheral vascular disease bypass surgery, or peripheral angioplasty surgery.

5. The method of claim 2, wherein said subject also has a history of at least one risk factor for cardiovascular disease.

6. The method of claim 1 or 5, wherein the risk factor is manifest coronary heart disease, coronary artery disease, thrombosis, transient ischaemic attack, left ventricular hypertrophy, arteriosclerosis, restenosis, tobacco smoking or peripheral vascular disease.

7. The method of claim 1 or 5, wherein the risk factor is elevated triglycerides, systemic inflammation, high blood phosphorus levels, high parathyroid hormone levels, microalbuminuria, or high homocysteine levels.

8. The method of claim 1 or 5, wherein the risk factor is obesity, hyperglycemia, chronic renal failure, high blood glucose, chronic kidney disease, or metabolic syndrome.

9. The method of claim 1 or 5, wherein the risk factor is hypertension, dyslipidemia, hyperlipidemia, elevated total cholesterol, elevated LDL cholesterol, or low HDL cholesterol or atherosclerosis.

10. The method of claim 1 or 2, wherein the subject has elevated levels of C-reactive protein (CRP).

11. The method of claim 1 or 2, wherein the subject is older than 55 years.

12. The method of claim 1 or 2, wherein the subject is non-hypertensive.

13. The method of claim 1 or 2, wherein the subject has diabetes mellitus.

14. The method of claim 13, wherein said diabetes mellitus is Type 2 diabetes.

15. The method of claim 1 or 2, wherein the subject has a history of two or more said risk factors.

16. The method of claim 15, wherein the subject has a history of three or more said risk factors.

17. The method of claim 1 or 2, wherein administering said therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof is sufficient to achieve a decrease in CRP levels.

18. A method of reducing mortality following a cardiovascular event in a subject, comprising administering to said subject a therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof.

19. The method of claim 18, wherein the cardiovascular event is myocardial infarction.

20. The method of claim 18, wherein the cardiovascular event is stroke.

21. The method of claim 18, wherein the cardiovascular event is congestive heart failure.

22. The method of claim 18, wherein the cardiovascular event is acute coronary syndrome.

23. The method of claim 18, wherein the cardiovascular event is angina.

24. The method of claim 18, wherein the cardiovascular event is a revascularization procedure.

25. The method of claim 24, wherein the revascularization procedure is a coronary, carotid or peripheral arterial revascularization procedure.

26. The method of claim 25, wherein the coronary, carotid or peripheral arterial revascularization procedure is a percutaneous coronary intervention (PCI), a stent implant, coronary artery bypass graft (CABG), carotid endarterectomy, peripheral vascular disease bypass surgery, or peripheral angioplasty surgery.

27. The method of claim 18, wherein the subject does not have Type 2 diabetes.

28. The method of claim 18, wherein the subject has survived a previous cardiovascular event of myocardial infarction or stroke.

29. The method of claim 18, wherein the occurrence of said cardiovascular event is a reoccurrence of a cardiovascular event of myocardial infarction or stroke.

30. The method of claim 18, wherein the subject has a history of one or more risk factors for cardiovascular disease.

31. The method of claim 30, wherein the risk factor is manifest coronary heart disease, coronary artery disease, thrombosis, transient ischaemic attack, left ventricular hypertrophy, arteriosclerosis, restenosis, tobacco smoking or peripheral vascular disease.

32. The method of claim 30, wherein the risk factor is elevated triglycerides, systemic inflammation, high blood phosphorus levels, high parathyroid hormone levels, microalbuminuria, or high homocysteine levels.

33. The method of claim 30, wherein the risk factor is obesity, hyperglycemia, chronic renal failure, high blood glucose, chronic kidney disease, or metabolic syndrome.

34. The method of claims 30, wherein the risk factor is hypertension, dyslipidemia, hyperlipidemia, elevated total cholesterol, elevated LDL cholesterol, or low HDL cholesterol or atherosclerosis.

35. The method of claim 18, wherein the subject is non-hypertensive.

36. The method of claim 30, wherein the subject has a history of two or more said risk factors.

37. The method of claim 36, wherein the subject has a history of three or more said risk factors.

38. The method of claim 18, wherein administering said therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof is sufficient to achieve a decrease in CRP levels.

39. A method of reducing a cardiovascular event in a subject with a history of at least one risk factor for cardiovascular disease, comprising administering to said subject a therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof, and wherein said risk factor is not Type 2 diabetes, obesity, hyperglycemia, dyslipidemia, hyperlipidemia, chronic renal failure, high blood glucose, chronic kidney disease, hypertension, atherosclerosis or metabolic syndrome.

40. The method of claim 39, wherein the risk factor is not Type 2 diabetes.

41. The method of claim 39 or 40, wherein the cardiovascular event is myocardial infarction.

42. The method of claim 39 or 40, wherein the cardiovascular event is stroke.

43. The method of claim 39 or 40, wherein the cardiovascular event is cardiac arrest.

44. The method of claim 39 or 40, wherein the cardiovascular event is congestive heart failure.

45. The method of claim 39 or 40, wherein the cardiovascular event is cardiovascular death.

46. The method of claim 39 or 40, wherein the cardiovascular event is acute coronary syndrome.

47. The method of claim 39 or 40, wherein the cardiovascular event is angina.

48. The method of claim 39 or 40, wherein the cardiovascular event is a revascularization procedure.

49. The method of claim 48, wherein the revascularization procedure is a coronary, carotid or peripheral arterial revascularization procedure.

50. The method of claim 49, wherein the coronary, carotid or peripheral arterial revascularization procedure is a percutaneous coronary intervention (PCI), a stent implant, coronary artery bypass graft (CABG), carotid endarterectomy, peripheral vascular disease bypass surgery, or peripheral angioplasty surgery.

51. The method of claim 39, wherein the risk factor is manifest coronary heart disease, coronary artery disease, thrombosis, transient ischaemic attack, left ventricular hypertrophy, arteriosclerosis, restenosis, tobacco smoking or peripheral vascular disease.

52. The method of claim 39, wherein the risk factor is elevated triglycerides, systemic inflammation, high blood phosphorus levels, high parathyroid hormone levels, microalbuminuria, or high homocysteine levels.

53. The method of claim 39, wherein the subject has elevated levels of C-reactive protein (CRP).

54. The method of claim 39, wherein the subject is older than 55 years.

55. The method of claim 39, wherein the subject has a history of two or more said risk factors.

56. The method of claim 55, wherein the subject has a history of three or more said risk factors.

57. The method of claim 39, wherein administering said therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof is sufficient to achieve a decrease in CRP levels.

58. A method of treating a cardiovascular event in a subject, wherein the cardiovascular event is myocardial infarction, stroke, congestive heart failure, acute coronary syndrome or angina, comprising administering to said subject a therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof and at least one other pharmaceutical composition comprising an active agent other than an IL-1β antibody or fragment.

59. The method of claim 58, wherein the active agent of said at least one other pharmaceutical composition is a cholesterol lowering agent, a statin, an HMG-CoA reductase inhibitor, a calcium channel blocker, a beta blocker, an antihypertensive, a

diuretic, aspirin, niacin, an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin II receptor blocker, a vasodilator, an anticoagulant, a inhibitor of platelet aggregation, a thrombolytic or digitalis.

60. A method for treating a cardiovascular event in a subject, wherein the cardiovascular event is myocardial infarction, stroke, congestive heart failure, acute coronary syndrome or angina, comprising administering to said subject a therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof and a revascularization procedure.

61. The method of claim 60, wherein the revascularization procedure is a coronary, carotid or peripheral arterial revascularization procedure.

62. A method of reducing restenosis in a subject following a revascularization procedure, comprising administering to said subject a therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof.

63. The method of claim 62, wherein the revascularization procedure is a coronary, carotid or peripheral arterial revascularization procedure.

64. The method of any one of claims 58, 60 or 62, wherein administering said therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof is sufficient to achieve a decrease in CRP levels.

65. A method of treating acute hypertension in a subject comprising administering to said subject a therapeutically effective amount of an anti-IL-1β binding antibody or binding fragment thereof and one or more antihypertensive agents.

66. The method of claim 65, wherein the subject has a blood pressure of greater than or equal to 180/110 mm Hg.

67. The method of claim 65, wherein the antihypertensive agent is administered intravenously.

68. The method of claim 65, wherein the antihypertensive agent is labetalol, metoprolol, hydralazine, nitroglycerin, nicardipine, sodium nitroprusside or clevidipine.

69. The method of any one of claims 1, 2, 18, 39, 60 or 62, further comprising administering at least one other pharmaceutical composition comprising an active agent other than an anti-IL-1β binding antibody or binding fragment thereof.

70. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is a cholesterol lowering agent.

71. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is a statin or an HMG-CoA reductase inhibitor.

72. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is a calcium channel blocker.

73. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is an antihypertensive, a diuretic or aspirin.

74. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker.

75. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is a vasodilator.

76. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is an anticoagulant or inhibitor of platelet aggregation.

77. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is a thrombolytic.

78. The method of claim 69, wherein the active agent of said at least one other pharmaceutical composition is digitalis.

79. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to human IL-1β with a dissociation constant of about 500 pM or less.

80. The method of claim 79, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to human IL-1β with a dissociation constant of about 50 pM or less.

81. The method of claim 80, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to human IL-1β with a dissociation constant of about 5 pM or less.

82. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof is a neutralizing antibody.

83. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to an IL-1β epitope such that the bound antibody or fragment substantially permits the binding of IL-1β to IL-1 receptor I (IL-1RI).

84. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof does not detectably bind to IL-1α, IL-1R or IL-1Ra.

85. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof competes with the binding of an antibody having the light chain variable region of SEQ ID NO:1 and the heavy chain variable region of SEQ ID NO:2

86. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to an epitope incorporating Glu64 of IL-1β.

87. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof binds to amino acids 1-34 of the N terminus of IL-1β.

88. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof is humanized or human.

89. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 1 mg/kg or less of antibody or fragment.

90. The method of claim 89, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 0.3 mg/kg or less of antibody or fragment.

91. The method of claim 90, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 0.03 mg/kg or less of antibody or fragment.

92. The method of any one of claims 89-91, wherein the one or more doses are at least 0.01 mg/kg of antibody or fragment.

93. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 0.03 mg/kg to 1 mg/kg.

94. The method of any one of claims 1-78, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered as a fixed dose, independent of a dose per subject weight ratio.

95. The method of claim 94, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 100 mg or less of antibody or fragment.

96. The method of claim 95, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 25 mg or less of antibody or fragment.

97. The method of claim 96, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 10 mg or less of antibody or fragment.

98. The method of any one of claims 94-97, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of at least 0.5 mg of antibody or fragment.

99. The method of claim 94 wherein the anti-IL-1β binding antibody or binding fragment thereof is administered in one or more doses of 1 mg to 100 mg of antibody or fragment.

100. The method of any one of claims 94-99, wherein said fixed dose of anti-IL-1β binding antibody or binding fragment thereof is administered using a pre-filled syringe or delivery device.

101. The method of any one of claims 1-100, wherein the anti-IL-1β binding antibody or binding fragment thereof is administered by subcutaneous, intravenous or intramuscular injection.

102. The method of any one of claims 1-101, wherein administration of an initial dose of anti-IL-1β binding antibody or binding fragment thereof is followed by the administration of one or more subsequent doses.

103. The method of claim 102, wherein said initial dose and one or more subsequent doses are administered at an interval of about once every week to about once every 12 months.

104. The method of claim 103, wherein said initial dose and one or more subsequent doses are administered at an interval of about once every two weeks to about once every 6 months.

105. The method of claim 104, wherein said initial dose and one or more subsequent doses are administered at an interval of about once every month to about once every 6 months.

106. The method of claim 105, wherein said initial dose and one or more subsequent doses are administered at an interval of about once every month to about once every 3 months.

107. The method of claim 105, wherein said initial dose and one or more subsequent doses are administered at an interval of about once every 3 months to about once every 6 months.