~~WHAT IS CLAIMED IS:~~ Claims:

1. A composition for use in a method of ~~preventing, slowing the progression of, arresting and/or reversing~~treating tissue calcification in a pre-diabetic subject or a subject with diabetes, with chronic kidney disease, or at risk of cardiovascular disease or a combination thereof, and in need thereof, ~~the method comprising administering to the subject at least 2 mg of substantially pure~~ wherein the composition comprises menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7~~) per day, thereby to prevent, slow the progression of, and/or arrest tissue calcification, wherein the~~ ), wherein at least 2 mg of the MK7 and/or MKH2-7 ~~is~~are administered ~~in a pharmaceutical composition.~~to the subject per day for at least 6 weeks, and whereupon the administration of the MK7 and/or MKH2-7:

(i) increases a plasma level of Fetuin A relative to the plasma level of Fetuin A prior to administration; or

(ii) decreases a plasma level of Highly Sensitive C Reactive Protein (hs-CRP) relative to the plasma level of hs-CRP prior to administration.

2. The ~~method~~composition for use of claim 1, wherein the subject has diabetes~~.~~

~~3. The method of claim 2, wherein the subject has~~ , such as type II diabetes~~.~~

~~4. The method of claim 1, wherein the subject~~ , or has been diagnosed as pre-diabetic.

~~5.~~ 3. The ~~method~~composition for use of ~~any one of claims~~claim 1~~-4~~, wherein the subject has chronic kidney disease~~.~~; or

~~6. The method of any one of claims 1-4, wherein the subject~~ has stage 4 or 5 chronic kidney disease/end stage renal disease.

~~7.~~ 4. The ~~method~~composition for use of ~~any one of claims~~claim 1~~-6~~, wherein the subject is undergoing hemodialysis.

~~8.~~ 5. The ~~method~~composition for use of ~~any one of claims~~claim 1~~-7~~, wherein the subject is receiving non-warfarin-based anti-coagulant therapy~~.~~

~~9. The method of claim 8, wherein the anti-coagulant therapy is~~ , such as oral anti-coagulation therapy~~.~~

~~10. The method of claim 9, wherein the anti-coagulation therapy comprises an inhibitor of Factor Xa activity (*e.g.*, apixaban, rivaroxaban, betrixaban, edoxaban, otamixaban, letaxaban, eribaxaban or fondaparinux) or Factor IIa activity (*e.g.*, dabigratran or argatroban).~~

~~11. A method of preventing, slowing the progression of, arresting~~, and~~/or reversing tissue calcification in a subject undergoing hemodialysis, and in need thereof, the method comprising administering to the subject at least 2 mg of substantially pure menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7) per day, thereby to prevent, slow the progression, arrest, and/or reverse tissue calcification, wherein the MK7 and/or MKH2-7 is administered in a pharmaceutical composition.~~

~~12. The method of claim 11, wherein the subject has diabetes.~~

~~13. The method of claim 12, wherein the diabetes is type II diabetes.~~

~~14. The method of claim 11, wherein the subject has been diagnosed as pre-diabetic.~~

~~15. The method of any one of claims 11-14, wherein the subject has chronic kidney disease.~~

~~16. The method of claim 15, wherein the subject has stage 4 or stage 5 chronic kidney disease/end stage renal disease.~~

~~17. The method of any one of claims 11-16, wherein the subject is receiving non-warfarin-based anticoagulant therapy.~~

~~18. The method of claim 17, wherein the anti-coagulant therapy is oral anti-coagulation therapy.~~

~~19. The method of claim 17,~~ and optionally wherein the anti-coagulation therapy comprises an inhibitor of Factor Xa activity ~~(*e.g.*, apixaban, rivaroxaban, betrixaban, edoxaban, or fondaparinux)~~ or Factor IIa activity ~~(*e.g.*, dabigratran or argatroban).~~.

~~20. A method of preventing, slowing the progression of, arresting, or reversing~~

6. A composition for use in a method of treating tissue calcification in a subject in need thereof, the composition comprising menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7), wherein the composition is administered wherein at least 2 mg of the MK7 and/or MKH2-7 are administered to the subject per day for at least 6 weeks, wherein the composition is a pharmaceutical composition, and wherein the administering the MK7 and/or MKH2-7 causes at least one of the following:

(i) increase the subject's serum T50 value relative to the subject's serum T50 value prior to administration of the MK-7 and/or MKH2-7,

(ii) increase a ratio of a carboxylated to a non-carboxylated form of a Vitamin K-dependent protein in the subject's plasma relative to the ratio prior to administration of the MK-7 and/or MKH2-7,

(iii) increase the plasma level of Fetuin A relative to the plasma concentration of Fetuin A prior to administration of the MK-7 and/or MKH2-7, or

(iv) decrease the plasma level of D-Dimer or Highly Sensitive C Reactive Protein relative to the plasma concentration of D-Dimer or Highly Sensitive C Reactive Protein (hs-CRP) prior to administration of the MK-7 and/or MKH2-7, thereby to treat tissue calcification in the subject; and wherein the subject:

(i) has diabetes;

(ii) has been diagnosed as pre-diabetic;

(iii) has chronic kidney disease; or

(iv) is undergoing hemodialysis.

7. The composition for use of claim 6, wherein the composition is for use in a method of treating tissue calcification in a subject with stage 5 chronic kidney disease and undergoing oral, non-warfarin-based anticoagulant therapy, and in need thereof, ~~the method comprising administering to the subject at least 2 mg of substantially pure menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7) per day, thereby to prevent, slow the progression of, arrest, and/or reverse tissue calcification in the subject, wherein the MK7 and/or MKH2-7 is administered in a pharmaceutical composition.~~and wherein upon administration of the MK7 and/or MKH2-7:

~~21.~~ (i) increases a plasma level of Fetuin A relative to the plasma level of Fetuin A prior to administration; or

(ii) decreases a plasma level of Highly Sensitive C Reactive Protein (hs-CRP) relative to the plasma level of hs-CRP prior to administration.

8. The ~~method~~composition for use of claim ~~20~~7, wherein the subject:

(i) is diabetic~~.~~;

~~22. The method of claim 20, wherein the subject~~(ii) has been diagnosed as pre-diabetic~~.~~; or

23. The method of any one of claims 21 or 22, wherein the subject(iii) is undergoing hemodialysis.

24. 9. The methodcomposition for use of any one of claims 21-23claim 7, wherein the anti-coagulation therapy comprises an inhibitor of Factor Xa activity (*e.g.*, apixaban, rivaroxaban, betrixaban, edoxaban, or fondaparinux) or Factor IIa activity (*e.g.*, dabigratran or argatroban).

25. 10. The method of any onecomposition for use of claim 1-24, whereupon administration of the MK-7 and/or MKH2-7 to the subject increases the subject's serum T50 value (*e.g.*, by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% or more) relative to the relative to the subject's serum T50 value prior to administration of the MK-7 and/or MKH2-7.

26. 11. The methodcomposition for use of any one of claimsclaim 1-25, wherein administration of the MK-7 and/or MKH2-

7-:

(a) increases a ratio of a carboxylated to a non-carboxylated of a Vitamin K dependent protein; or

(b) decreases an amount of a non-carboxylated Vitamin K dependent protein in plasma of the subject relative to the ratio or amount present prior to administration of the MK-7 and/or MKH2-7. MKH2-7.

27. 12. The methodcomposition for use of claim 2611, wherein the Vitamin K-dependent protein is selected from Matrix Gla Protein, Growth Arrest Specific Gene 6 (Gas-6) protein, PIVKA-II protein, osteocalcin, activated Protein C, or activated Protein S.

28. The method of any one of claims 1-27, wherein upon administration of the MK-7 and/or MKH2-7 to the subject increases a plasma level of osteoprotegerin or Fetuin A relative to the plasma level of osteoprotegerin or Fetuin A prior to administration of the MK-7 and/or MKH2-7.

29. 13. The method of any one of claims 1-28 The composition for use of claim 1, wherein upon administration of the MK-7 and/or MKH2-7 to the subject decreases a plasma level of D-Dimer or Highly Sensitive C Reactive Protein (hs-CRP) relative to the plasma level of D-Dimer or Highly Sensitive C Reactive Protein (hs-CRP) prior to administration of the MK-7 and/or MKH2-7.

30. 14. The methodcomposition for use of any one of claimsclaim 1-29, wherein, when the subject has a dermal lesion and/or vascular lesion, the administration of the MK-7 and/or MKH2-7 reduces the size of the dermal and/or vascular lesion.

31. The method of claim 30, wherein administration of the MK-7 and/or MKH2-7 reduces the total surface area of the lesion by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%.

32. A method of preventing, slowing the progression of, arresting, and/or reversing tissue calcification in a subject in need thereof, the method comprising administering to the subject at least 2 mg of substantially pure menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7) per day, wherein the MK7 and/or MKH2-7 is administered in a pharmaceutical composition, so as to cause at least one of the following:

(i) increase the subject's serum T50 value (*e.g.*, by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% or more) relative to the subject's serum T50 value prior to administration of the MK-7 and/or MKH2-7,

(ii) increase a ratio of a carboxylated to a non-carboxylated form of a Vitamin K-dependent protein in the subject's plasma (*e.g.*, by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% or more) relative to the ratio prior to administration of the MK-7 and/or MKH2-7,

(iii) increase the plasma level of osteoprotegerin or Fetuin A (*e.g.*, by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% or more) relative to the plasma concentration of osteoprotegerin or Fetuin A prior to administration of the MK-7 and/or MKH2-7, or

(iv) decrease the plasma level of D-Dimer or Highly Sensitive C Reactive Protein (hs-CRP) (*e.g.*, by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%) relative to the plasma concentration of D-Dimer or Highly Sensitive C Reactive Protein (hs-CRP) prior to administration of the MK-7 and/or MKH2-7,

thereby to prevent, slow the progression of, arrest and/or reverse tissue calcification in the subject.

33. The method of claim 32, wherein the subject has diabetes.

34. The method of claim 32, wherein the subject has been diagnosed as pre-diabetic.

35. The method of claim 32 or 33, wherein the subject has chronic kidney disease.

36. The method of any one of claims 32-35, wherein the subject is undergoing hemodialysis.

37. The method of any one of claims 32-36, wherein the subject is receiving non-warfarin-based anti-coagulant therapy.

38. The method of claim 37, wherein the anti-coagulant therapy is oral anti-coagulation therapy.

39. The method of claim 38, wherein the anti-coagulation therapy comprises an inhibitor of Factor Xa activity (*e.g.*, apixaban, rivaroxaban, betrixaban, edoxaban, or fondaparinux) or Factor IIa activity (*e.g.*, dabigratran or argatroban).

40. The method of any one of claims 33-39, wherein the Vitamin K-dependent protein is selected from Matrix Gla protein, Growth Arrest Specific Gene 6 (Gas-6) protein, PIVKA-II protein, osteocalcin, activated Protein C, or activated Protein S.

41. The method of any one of claims 1-40, comprising administering from about 2 mg to about 100 mg of MK-7 and/or MKH2-7 to the subject per day.

42. The method of any one of claims 1-41, comprising administering from about 5 mg to about 100 mg of MK-7 and/or MKH2-7 to the subject per day.

43. The method of any one of claims 1-42, comprising administering from about 10 mg to about 100 mg of MK-7 and/or MKH2-7 to the subject per day.

44. The method of any one of claims 1-43, comprising administering 10, 25, 50, 75, 100 mg or more of MK-7 and/or MKH2-7 to the subject per day.

45. The method of any one of claims 1-44, wherein the MK-7 and/or MKH2-7 is administered to the subject for at least 2 weeks.

46. The method of any one of claims 1-45, wherein the MK-7 and/or MKH2-7 is administered to the subject for at least 6 weeks.

47. The method of any one of claims 1-46, wherein, if the subject is undergoing hemodialysis, the MK-7 and/or MKH2-7 is administered to the subject for a period that includes the duration of hemodialysis.

48. The method of any one of claims 1-47, wherein the MK-7 and/or MKH2-7 is administered orally.

49. The method of any one of claims 1-48, wherein the MK-7 and/or MKH2-7 is disposed within a tablet, caplet or capsule.

50. The method of any one of claims 1-49, wherein the subject has previously been exposed to warfarin-based anti-coagulation therapy.

51. The method of any one of claims 1-50, wherein the subject is receiving a statin.

52. The method of claim 51, wherein the statin is selected from simvastatin, lovastatin, atorvastatin, pravastatin, pitavastatin, rosuvastatin, and fluvastatin.

53. The method of any one of claims 1-52, wherein the tissue calcification is vascular calcification.

54. The method of any one of claims 1-53, wherein the tissue calcification is dermal calcification.

55. A method of preventing, slowing the progression of, arresting, and/or reversing tissue calcification in a subject in need thereof, the method comprising administering to the subject

(a) at least 2 mg of substantially pure menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7) per day; and

(b) a statin.

56. The method of claim 55, wherein the statin is selected from simvastatin, lovastatin, atorvastatin, pravastatin, pitavastatin, rosuvastatin, and fluvastatin.

57. The method of claim 55 or 56, wherein the MK-7 and/or MKH2-7 is administered in the same dosage form as the statin.

58. The method of claim 55 or 56, wherein the MK-7 and/or MKH2-7 is administered in a separate dosage form from the statin.

59. A method of improving aortic compliance in a subject in need thereof, the method comprising administering to the subject an effective amount of substantially pure menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7) per day.

60. A method of stopping and/or reversing peripheral vasculopathy in a subject in need thereof, wherein the subject has ESRD or CKD, the method comprising administering to the

~~subject an effective amount of substantially pure menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7) per day.~~

~~61. A method of preventing, slowing the progression of, arresting, and/or reversing one or more symptoms of chronic obstructive pulmonary disease (COPD) in a subject in need thereof, the method comprising administering to the subject at least 2 mg of substantially pure menaquinone-7 (MK-7) and/or menaquinol-7 (MKH2-7) per day, thereby to prevent, or slow the progression of, arrest, and/or reverse the one or more symptoms of COPD, wherein the MK7 and/or MKH2-7 is administered in a pharmaceutical composition.~~

~~62. The method of claim 61, wherein the one or more symptoms is selected from the group consisting of breathing difficulty, cough, mucus production, wheezing, and elastinolysis.~~

~~63. The method of claim 59-62, comprising administering from about 2 mg to about 100 mg of MK-7 and/or MKH2-7 to the subject per day.~~

~~64. The method of any one of claims 59-63, comprising administering from about 5 mg to about 100 mg of MK-7 and/or MKH2-7 to the subject per day.~~

~~65. The method of any one of claims 59-64, comprising administering from about 10 mg to about 100 mg of MK-7 and/or MKH2-7 to the subject per day.~~

~~66. The method of any one of claims 59-65, comprising administering 10, 25, 50, 75 or 100 mg of MK-7 and/or MKH2-7 to the subject per day.~~

~~67. The method of any one of claims 59-66, wherein the MK-7 and/or MKH2-7 is administered to the subject for at least 2 weeks.~~

~~68. The method of any one of claims 59-67, wherein the MK-7 and/or MKH2-7 is administered to the subject for at least 6 weeks.~~

~~69. The method of any one of claims 59-67, wherein the MK-7 and/or MKH2-7 is administered to the subject indefinitely.~~

~~70. The method of any one of claims 59-69, wherein the MK-7 and/or MKH2-7 is administered orally.~~

~~71. The method of any one of claims 59-70, wherein the MK-7 and/or MKH2-7 is disposed within a tablet, caplet or capsule.~~

~~72. The method of any one of claims 59-71, wherein the subject is receiving a statin.~~

~~73. The method of claim 72, wherein administration of the MK-7 and/or MKH2-7 prevents or decreases the Vitamin K-depleting effects of the statin.~~