

## CLAIMS

## WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising
  - (a) an extracellular vesicle;
  - (b) a saccharide;
  - (c) sodium chloride;
  - (d) a potassium phosphate; and
  - (e) a sodium phosphate,wherein the composition is in a solution at a pH of about 7.2.
2. The composition of claim 1, wherein the extracellular vesicle is an exosome.
3. The composition of claim 1 or claim 2, wherein the composition is capable of being stored for at least about 4 hours, at least about 5 hours, at least about 6 hours, at least about 7 hours, at least about 8 hours, at least about 9 hours, at least about 10 hours, at least about 11 hours, at least about 12 hours, at least about 15 hours, at least about 20 hours, at least about 24 hours, at least about 2 days, at least about 3 days, at least about 4 days, at least about 5 days, at least about 6 days, or at least about 7 days at a temperature of 4 °C.
4. The composition of any one of claims 1 to 3, wherein the composition is capable of being frozen and thawed, wherein the thawed composition has a pH of about 7.2.
5. The composition of any one of claims 1 to 4, wherein the composition has a pH of 7.0, 7.1, 7.2, 7.3, or 7.4.
6. The composition of any one of claims 1 to 5, wherein the composition has a pH of 7.2.
7. The composition of any one of claims 1 to 6, wherein the pI is in the range of about 1 to about 6.5.

8. The composition of any one of claims 1 to 7, wherein the composition has (i) reduced aggregates, (ii) improved stability of the EV, (iii) improved integrity of the EV architecture, and (iv) improved stability of engineered proteins contained on or in EVs.

9. The composition of any one of claims 1 to 8, wherein the saccharide comprises a monosaccharide, a disaccharide, a trisaccharide, an oligosaccharide, a polysaccharide, a sugar alcohol, or any combination thereof.

10. The composition of any one of claims 1 to 9, wherein the saccharide has a molecular weight of from about 180.00 g/mol to about 380.00 g/mol.

11. The composition of any one of claims 1 to 10, wherein the saccharide comprises lactose, glucose, sucrose, trehalose, and/or combinations thereof.

12. The composition of any one of claims 1 to 11, wherein the saccharide is a sugar alcohol having a molecular weight of from about 90.00 g/mol to about 190.00 g/mol.

13. The composition of any one of claims 9 to 12, wherein the sugar alcohol comprises glycerol, sorbitol, mannitol, xylitol, and/or combinations thereof.

14. The composition of any one of claims 1 to 13, wherein the saccharide is a sucrose or a trehalose.

15. The composition of any one of claims 1 to 14, wherein the saccharide is present in the composition at a concentration of about 5% w/v.

16. A pharmaceutical composition comprising (i) an extracellular vesicle and (ii) a saccharide, which is a sucrose or a trehalose at a concentration of about 5% w/v.

17. The composition of claim 16, wherein the composition has improved stability compared to a reference composition comprising a sucrose or a trehalose at a concentration of 1% w/v to 4% w/v.

18. The composition of any one of claims 1 to 17, wherein the composition has a conductivity between about 6 mS/cm +/- 10% and about 10 mS/cm +/- 10%.

19. The composition of claim 18, wherein the conductivity is between 6 mS/cm and about 7 mS/cm, between about 7 mS/cm and about 8 mS/cm, between about 8 mS/cm and about 9 mS/cm, or between about 9 mS/cm and about 10 mS/cm.

20. The composition of claim 18 or 19, wherein the conductivity is about 6 mS/cm, about 7 mS/cm, about 8 mS/cm, about 9 mS/cm, or about 10 mS/cm.

21. The composition of any one of claims 16 to 20, which further comprises sodium chloride.

22. The composition of any one of claims 1 to 15 and 16 to 21, wherein the sodium chloride is present in the composition at a concentration of between about 10 mM and about 134 mM.

23. The composition of claim 22, wherein the concentration of sodium chloride is between about 10 mM to about 130 mM, between about 20 mM to about 120 mM, between about 30 mM to about 110 mM, between about 40 mM to about 100 mM, between about 50 mM to about 90 mM, between about 60 mM to about 80 mM, between about 70 mM to about 80 mM, between about 45 mM to about 95 mM, between about 45 mM to about 80 mM, between about 45 mM to about 70 mM, between about 45 mM to about 65 mM, between about 50 mM to about 65 mM, between about 50 mM to about 60 mM, between about 50 mM to about 55 mM, between about 50 mM to about 55 mM, or between about 51 mM to about 54 mM.

24. The composition of claim 22 or 23, wherein the concentration of sodium chloride is about 10 mM, about 20 mM, about 30mM, about 40mM, about 50 mM, about 60 mM, about 70 mM, about 80 mM, about 90 mM, or about 100 mM.

25. The composition of any one of claims 22 to 24, wherein the concentration of sodium chloride is about 39 mM, about 40 mM, about 41 mM, about 42 mM, about 43 mM, about 44 mM, about 45 mM, about 46 mM, about 47 mM, about 48 mM, about 49 mM, or about 50 mM.

26. The composition of any one of claims 16 to 25, wherein the composition further comprises a phosphate buffer.

27. The composition of claim 26, wherein the phosphate buffer comprises at least one phosphate compound comprising potassium phosphate, sodium phosphate, disodium hydrogen

phosphate, potassium dihydrogen phosphate, dipotassium phosphate, and/or a combination thereof.

28. The composition of claim 27, wherein the phosphate buffer comprises a potassium phosphate and a sodium phosphate at a ratio of about 1: about 2, about 1: about 3, about 1: about 4; or about 1: about 5.

29. The composition of claim 27 or 28, wherein the phosphate buffer comprises a potassium phosphate and a sodium phosphate at a ratio of about 1: about 3.

30. The composition of any one of claims 27 to 29, wherein the phosphate buffer comprises a potassium phosphate and a sodium phosphate at a ratio of about 1: about 2.

31. A pharmaceutical composition comprising (i) an extracellular vesicle, (ii) a potassium phosphate, and (iii) a sodium phosphate in a solution, wherein the ratio of the potassium phosphate and the sodium phosphate is about 1 to about 3 or about 1 to about 2.

32. The composition of any one of claims 16 to 31, wherein the solution has a pH of 7.1 to 7.3.

33. The composition of any one of claims 1 to 15 and 27 to 32, wherein the potassium phosphate is present in the composition at a concentration of between about 1 mM to about 20 mM, between about 2 mM to about 19 mM, between about 3 mM to about 18 mM, between about 4 mM to about 17 mM, between about 5 mM to about 16 mM, or between about 5 mM to about 15 mM.

34. The composition of claim 33, wherein the concentration of the potassium phosphate is about 4.5 mM, about 4.6 mM, about 4.7 mM, about 4.8 mM, about 4.9 mM, about 5.0 mM, about 5.1 mM, about 5.2 mM, about 5.3 mM, about 5.4 mM, or about 5.5 mM.

35. The composition of claim 33 or 34, wherein the concentration of the potassium phosphate is 5.15 mM.

36. The composition of claim 33, wherein the concentration of the potassium phosphate is about 15.0 mM, about 15.1 mM, about 15.2 mM, about 15.3 mM, about 15.4 mM, about 15.5

mM, about 15.6 mM, about 15.7 mM, about 15.8 mM, about 15.9 mM, about 16.0, about 16.1 mM, about 16.2 mM, about 16.3 mM, about 16.4 mM, or about 16.5 mM.

37. The composition of claim 33 or 36, wherein the concentration of the potassium phosphate is 15.4 mM.

38. The composition of any one of claims 1 to 15 and 27 to 37, wherein the potassium phosphate is potassium phosphate monobasic.

39. The composition of any one of claims 1 to 15 and 27 to 38, wherein the sodium phosphate is present in the composition at a concentration of between about 10 mM to about 30, between about 11 mM to about 29 mM, between about 12 mM to about 28 mM, between about 13 mM to about 27 mM, or between about 14 mM to about 26 mM.

40. The composition of claim 39, wherein the sodium phosphate is present in the composition at a concentration of about 14.5 mM, about 14.6 mM, about 14.7 mM, about 14.8 mM, about 14.9 mM, about 15.0 mM, about 15.1 mM about 15.2 mM, about 15.3 mM, about 15.4, mM, or about 15.5 mM.

41. The composition of claim 39 or 40, wherein the concentration of the sodium phosphate is 14.9 mM.

42. The composition of claim 39, wherein the sodium phosphate is present in the composition at a concentration of about 26.5 mM, about 26.6 mM, about 26.7 mM, about 26.8 mM, about 26.9 mM, about 27.0 mM, about 27.1 mM about 27.2 mM, about 27.3 mM, about 27.4, mM, or about 27.5 mM.

43. The composition of claim 39 or 42, wherein the concentration of the sodium phosphate is 27.1 mM.

44. The composition of any one of claims 1 to 15 and 27 to 43, wherein the sodium phosphate is sodium phosphate dibasic heptahydrate.

45. The composition of any one of claims 1 to 44, further comprising an anti-oxidant.

46. The composition of 45, wherein the anti-oxidant comprises D-methionine, L-methionine, ascorbic acid, erythorbic acid, Na ascorbate, thioglycerol, cysteine, acetylcysteine,

cystine, dithioerythritol, glutathione, tocopherols, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), sodium bisulphate, sodium dithionite, A-Tocopherol,  $\gamma$ -Tocopherol, propyl gallate, ascorbyl palmitate, sodium metabisulfite, thiourea, sodium thiosulfate, propyl gallate, and sodium thioglycolate.

47. The composition of any one of claims 1 to 46, wherein the composition is not lyophilized.

48. The composition of any one of claims 1 to 47, wherein the composition does not comprise a chelating agent.

49. The composition of any one of claims 1 to 48, wherein the composition does not comprise albumin.

50. The composition of any one of claims 1 to 49, comprising

- a. a sucrose at a concentration of about 5% w/v,
- b. sodium chloride at a concentration of about 50 mM;
- c. a potassium phosphate monobasic at a concentration of about 5 mM;
- d. a sodium phosphate dibasic heptahydrate at a concentration of about 15mM;

wherein the composition is in a solution at a pH of 7.2 and at a conductivity of 7.23 mS/cm +/- 10%.

51. The composition of any one of claims 1 to 49, comprising,

- a. a sucrose at a concentration of about 5% w/v,
- b. sodium chloride at a concentration of about 40 mM;
- c. a potassium phosphate monobasic at a concentration of about 15 mM;
- d. a sodium phosphate dibasic heptahydrate at a concentration of about 27 mM;

wherein the composition is in a solution at a pH of 7.2 and at a conductivity of 8.8 mS/cm +/- 10%.

52. The composition of any one of claims 1 to 51, wherein the composition is capable of being stored at a temperature of from about -20 °C to about -80 °C, wherein the stability of the extracellular vesicle is not reduced.

53. The composition of claim 52, wherein the composition can be stored for about one week, about two weeks, about three weeks, about four weeks, about one month, about two months, about three months, about four months, about five months, about six months, about seven months, about eight months, about nine months, about ten months, about 11 months, about 12 months, about one year, about two years, about three years, or about four years.

54. The composition of any one of claims 16 to 53, wherein the extracellular vesicle is an exosome.

55. The composition of any one of claims 1 to 15 and 16 to 54, wherein the extracellular vesicle further comprises a scaffold protein.

56. The composition of claim 55, wherein the scaffold protein is Scaffold X.

57. The composition of claim 55 or 56, wherein a payload is linked to the scaffold protein.

58. The composition of claim 57, wherein the payload is linked to the scaffold protein by a linker.

59. The composition of claim 58, wherein the linker is a polypeptide.

60. The composition of claim 58, wherein the linker is a non-polypeptide moiety.

61. The composition of any one of claims 56 to 60, wherein Scaffold X is a scaffold protein that is capable of anchoring the payload on the exterior surface of the extracellular vesicle.

62. The composition of any one of claims 56 to 61, wherein the scaffold protein comprises prostaglandin F2 receptor negative regulator (the PTGFRN protein).

63. The composition of any one of claims 55 to 62, wherein the scaffold protein comprises the PTGFRN protein or a fragment thereof.

64. The composition of claim 55 to 62, wherein the scaffold protein comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1-7 and 33.

65. The composition of any one of claims 55 to 64, wherein the scaffold protein comprises an amino acid sequence at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or about 100% identical to SEQ ID NO: 1.

66. The composition of claim 1 to 67, wherein the extracellular vesicle comprises a biologically active moiety.

67. The composition of claim 55 to 68, wherein the scaffold protein is fused to the biologically active moiety.

68. The composition of claim 55 to 68, wherein the scaffold protein is not fused to the biologically active moiety.

69. The composition of any one of claims 68 to 71 wherein the biologically active moiety comprises a STING agonist.

70. The composition of claim 71, wherein the STING agonist comprises CL656.

71. The composition of claim 72, wherein the STING agonist is isomer A, isomer B, isomer C, or isomer D of CL656.

72. The composition of any one of claims 71 to 73, wherein the STING agonist is not fused to the scaffold protein.

73. The composition of any one of claims 68 to 70, wherein the biologically active moiety is IL-12, CD40L, FLT3L, or any combination thereof.

74. The composition of claim 75, wherein the biologically active moiety is fused to the scaffold protein.

75. The composition of any one of claims 1 to 76, wherein the composition can be administered by a parenteral, topical, intravenous, oral, subcutaneous, intra-arterial, intradermal,

transdermal, rectal, intracranial, intraperitoneal, intranasal, intratumoral, intramuscular route, or as an inhalant.

76. A method of preparing the pharmaceutical composition of any one of claims 1 to 77 comprising combining:

- (a) an extracellular vesicle;
- (b) a saccharide;
- (c) sodium chloride;
- (d) a potassium phosphate; and
- (e) a sodium phosphate,

77. The method of claim 78, wherein the extracellular vesicle is an exosome.

78. A method of preparing a pharmaceutical composition comprising combining an extracellular vesicle and a saccharide, which is a sucrose or trehalose at a concentration of about 5% w/v, wherein the composition exhibits improved stability compared to a composition comprising sucrose or trehalose at a concentration of 1 to 4%.

79. A method of preparing a pharmaceutical composition comprising combining an extracellular vesicle and a phosphate compound, wherein the phosphate compound comprises a potassium phosphate and a sodium phosphate at a ratio that gives rise to a pH between 7.1 and 7.3.

80. The method of any one of claims 78 to 81, wherein the conductivity of the composition is further adjusted.

81. The method of claim 97, wherein the conductivity of the composition is between about 7.1 to about 7.3 mS/cm.

82. The method of claim 83, wherein the conductivity is 7.23 mS/cm.

83. A method of treating a disease or a condition in a subject in need thereof comprising administering to the subject the composition of any one of claims 1 to 77.

84. The method of claim 85, wherein the disease or condition is a cancer, a fibrosis, a hemophilia, diabetes, a growth factor deficiency, an eye disease, a Pompe disease, a lysosomal storage disorder, mucoviscidosis, cystic fibrosis, Duchenne and Becker muscular dystrophy, transthyretin amyloidosis, hemophilia A, hemophilia B, adenosine-deaminase deficiency, Leber's congenital amaurosis, X-linked adrenoleukodystrophy, metachromatic leukodystrophy, OTC deficiency, glycogen storage disease 1A, Crigler-Najjar syndrome, primary hyperoxaluria type 1, acute intermittent porphyria, phenylketonuria, familial hypercholesterolemia, mucopolysaccharidosis type VI,  $\alpha$ 1 antitrypsin deficiency, and a hypercholesterolemia.

85. The method of claim 86 wherein the cancer is bladder cancer, cervical cancer, renal cell cancer, testicular cancer, colorectal cancer, lung cancer, head and neck cancer, ovarian, lymphoma, liver cancer, glioblastoma, melanoma, myeloma, leukemia, pancreatic cancer, or combinations thereof.

86. The pharmaceutical composition of any one of claims 1 to 77 for treating a disease or a condition in a subject in need thereof.

87. Use of the composition of any one of claims 1 to 77 in the manufacture of a medicament for treating a disease or a condition.

88. The composition of any one of claims 1 to 68, comprising:

- (a) Extracellular vesicles;
- (b) Sucrose at a concentration between about 4% w/v and about 6% w/v, e.g., 5 % w/v;
- (c) Sodium chloride at a concentration between 30 mM and about 50 mM;
- (d) Potassium phosphate monobasic at a concentration between about 5 mM and about 25 mM;
- (e) Sodium phosphate dibasic heptahydrate at a concentration between about 15 mM and about 35 mM,
- (f) wherein the pH of the composition is from about 6.7 to about 7.7.

89. The composition of claim 88, comprising

- (a) Extracellular vesicles;
- (b) Sucrose at a concentration of about 5 % w/v;
- (c) Sodium chloride at a concentration of about 40 mM;

- (d) Potassium phosphate monobasic at a concentration of about 15 mM;
- (e) Sodium phosphate dibasic heptahydrate at a concentration of about 27 mM,
- (f) wherein the pH of the composition is about 7.2.

90. The composition of claim 88 or 89, wherein the extracellular vesicles comprise a STING agonist.

91. The composition of one of claims 1 to 68, comprising:

- (a) Extracellular vesicles;
- (b) Sucrose at a concentration from at least about 50 mM to at least about 300 mM;
- (c) Sodium chloride at a concentration from at least about 10 mM to at least about 200 mM;
- (d) Potassium phosphate monobasic at a concentration from at least about 1 mM to at least about 20 mM;
- (e) Sodium phosphate dibasic at a concentration from at least about 5 mM to at least about 35 mM,
- (f) wherein the pH of the composition is from about 6.7 to about 7.7.

92. The composition of claim 91, comprising:

- (a) Extracellular vesicles;
- (b) Sucrose at a concentration of about 146 mM;
- (c) Sodium chloride at a concentration of about 50 mM;
- (d) Potassium phosphate monobasic at a concentration of about 5 mM;
- (e) Sodium phosphate dibasic at a concentration of about 15 mM, and
- (f) wherein the pH of the composition is about 7.2.

93. The composition of one of claims 1 to 68, comprising:

- (a) Extracellular vesicles;
- (b) Sucrose at a concentration from at least about 1% to at least about 10%;
- (c) Sodium chloride at a concentration from at least about 10 mM to at least about 200 mM;
- (d) Potassium phosphate monobasic at a concentration from at least about 1 mM to at least about 20 mM;

- (e) Sodium phosphate dibasic at a concentration from at least about 5 mM to at least about 35 mM,
- (f) wherein the pH of the composition is from about 6.7 to about 7.7.

94. The composition of claim 93, comprising:

- (a) Extracellular vesicles;
- (b) Sucrose at a concentration of about 5%;
- (c) Sodium chloride at a concentration of about 50 mM;
- (d) Potassium phosphate monobasic at a concentration of about 5 mM;
- (e) Sodium phosphate dibasic at a concentration of about 15 mM, and
- (f) wherein the pH of the composition is about 7.2.

95. The composition of any one of claims 91 to 94, wherein the extracellular vesicles comprise an IL-12 moiety.

96. The composition of claim 95, wherein the IL-12 moiety comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or 100% identical to the amino acid sequence set forth in SEQ ID NO: 11, 12, or 13.

97. The composition of claim 95 or 96, wherein the IL-12 moiety comprises the amino acid sequence set forth in SEQ ID NO: 13.

98. The composition of any one of claims 1 to 68, comprising:

- (a) Extracellular vesicles comprising an ASO;
- (b) Sucrose;
- (c) Sodium chloride;
- (d) Potassium phosphate monobasic at a concentration of about 5 mM;
- (e) Sodium phosphate dibasic at a concentration of about 15 mM, and
- (f) wherein the pH of the composition is about 7.2;

wherein the sucrose is at a concentration selected from about 73 mM, about 80 mM, about 85 mM, about 90 mM, about 95 mM, about 100 mM, about 105 mM, about 110 mM, about 115 mM, about 120 mM, about 125 mM, about 130 mM, about 135 mM, about 140 mM, about 145 mM, about 146 mM, and about 150 mM; and

wherein the sodium chloride is at a concentration selected from about 50 mM, about 55 mM, about 60 mM, about 65 mM, about 70 mM, about 75 mM, about 80 mM, about 85 mM, about 90 mM, about 95 mM, about 100 mM, about 105 mM, about 110 mM, about 115 mM, about 120 mM, about 125 mM, about 130 mM, about 135 mM, about 140 mM, about 145 mM, about 146 mM, and about 150 mM.

99. The composition of any one of claims 1 to 68, comprising:

- (a) Extracellular vesicles comprising an ASO;
- (b) Sucrose;
- (c) Sodium chloride;
- (d) Potassium phosphate monobasic at a concentration of about 5 mM;
- (e) Sodium phosphate dibasic at a concentration of about 15 mM, and
- (f) wherein the pH of the composition is about 7.2;

wherein the sucrose is at a concentration selected from about 2.5%, about 2.6%, about 2.7%, about 2.8%, about 2.9%, about 3.0%, about 3.1%, about 3.2%, about 3.3%, about 3.4%, about 3.5%, about 3.6%, about 3.7%, about 3.8%, about 3.9%, about 4.0%, about 4.1%, about 4.2%, about 4.3%, about 4.4%, about 4.5%, about 4.6%, about 4.7%, about 4.8%, about 4.9%, and about 5.0%; and

wherein the sodium chloride is at a concentration selected from about 50 mM, about 55 mM, about 60 mM, about 65 mM, about 70 mM, about 75 mM, about 80 mM, about 85 mM, about 90 mM, about 95 mM, about 100 mM, about 105 mM, about 110 mM, about 115 mM, about 120 mM, about 125 mM, about 130 mM, about 135 mM, about 140 mM, about 145 mM, about 146 mM, and about 150 mM.

100. The composition of claim 98 or 99, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193

101. The composition of any one of claims 1 to 68, comprising:

- (a) Extracellular vesicles comprising an ASO, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193;
- (b) Sucrose at a concentration of about 73 mM to about 146 mM;
- (c) Sodium chloride at a concentration of about 50 mM to about 150 mM;
- (d) Potassium phosphate monobasic at a concentration of about 5 mM;

- (e) Sodium phosphate dibasic at a concentration of about 15 mM,
  - (f) wherein the pH of the composition is about 7.2.
102. The composition of any one of claims 1 to 68, comprising:
- (a) Extracellular vesicles comprising an ASO, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193;
  - (b) Sucrose at a concentration of about 2.5% to about 5%;
  - (c) Sodium chloride at a concentration of about 50 mM to about 150 mM;
  - (d) Potassium phosphate monobasic at a concentration of about 5 mM;
  - (e) Sodium phosphate dibasic at a concentration of about 15 mM,
  - (f) wherein the pH of the composition is about 7.2.
103. The composition of any one of claims 1 to 68, comprising:
- (a) Extracellular vesicles comprising an ASO, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193;
  - (b) Sucrose at a concentration of about 146 mM;
  - (c) Sodium chloride at a concentration of about 50 mM;
  - (d) Potassium phosphate monobasic at a concentration of about 5 mM;
  - (e) Sodium phosphate dibasic at a concentration of about 15 mM,
  - (f) wherein the pH of the composition is about 7.2.
104. The composition of any one of claims 1 to 68, comprising:
- (a) Extracellular vesicles comprising an ASO, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193;
  - (b) Sucrose at a concentration of about 5%;
  - (c) Sodium chloride at a concentration of about 50 mM;
  - (d) Potassium phosphate monobasic at a concentration of about 5 mM;
  - (e) Sodium phosphate dibasic at a concentration of about 15 mM,
  - (f) wherein the pH of the composition is about 7.2.
105. The composition of any one of claims 1 to 68, comprising:
- (a) Extracellular vesicles comprising an ASO, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193;
  - (b) Sucrose at a concentration of about 2.5%;

- (c) Sodium chloride at a concentration of about 50 mM;
  - (d) Potassium phosphate monobasic at a concentration of about 5 mM;
  - (e) Sodium phosphate dibasic at a concentration of about 15 mM,
  - (f) wherein the pH of the composition is about 7.2.
106. The composition of any one of claims 1 to 68, comprising:
- (a) Extracellular vesicles comprising an ASO, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193;
  - (b) Sucrose at a concentration of about 5%;
  - (c) Sodium chloride at a concentration of about 100 mM;
  - (d) Potassium phosphate monobasic at a concentration of about 5 mM;
  - (e) Sodium phosphate dibasic at a concentration of about 15 mM,
  - (f) wherein the pH of the composition is about 7.2.
107. The composition of any one of claims 1 to 68, comprising:
- (a) Extracellular vesicles comprising an ASO, wherein the ASO comprises a nucleic acid sequence selected from SEQ ID NOs: 91-193;
  - (b) Sucrose at a concentration of about 2.5%;
  - (c) Sodium chloride at a concentration of about 100 mM;
  - (d) Potassium phosphate monobasic at a concentration of about 5 mM;
  - (e) Sodium phosphate dibasic at a concentration of about 15 mM,
  - (f) wherein the pH of the composition is about 7.2.
108. The composition of any one of claims 98 to 107, wherein the ASO comprises the nucleic acid sequence set forth in SEQ ID NO: 144.
109. The composition of any one of claims 98 to 107, wherein the ASO comprises the nucleic acid sequence set forth in SEQ ID NO: 145.
110. The composition of any one of claims 98 to 107, wherein the ASO comprises the nucleic acid sequence set forth in SEQ ID NO: 193.
111. The composition of any one of claims 98 to 107, wherein the ASO comprises the nucleic acid sequence set forth in SEQ ID NO: 185.

112. The composition of any one of claims 98 to 111, wherein the ASO is associated with the extracellular vesicles by a linker.

113. The composition of claim 112, wherein the linker comprises cholesterol, tocopherol, a fatty acid, or any combination thereof.

114. The composition of claim 112 or 113, wherein the linker is a cleavable linker.

115. The composition of any one of claims 58 to 60, wherein the linker is a cleavable linker.