WHAT IS CLAIMED IS

1. A conjugate comprising:

a scaffold protein, a membrane-forming lipid, and an antigen-binding polypeptide,

wherein said membrane-forming lipids arrange in a lipid bilayer and said scaffold protein encircles said bilayer; and

wherein said antigen-binding polypeptide is conjugated to one or more of said membrane-forming lipids on one or both surfaces of said bilayer via a functionalized group on said one or more membrane-forming lipids and a complementary functional group located C-terminally on said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide.

~~2. The conjugate of claim 1, wherein said functionalized group is selected from the group consisting of a maleimide derivative, a haloacetamide, a pyridyldithio propionate, a thiosulfate, and a combination of any one or more thereof; and said complementary functional group is a free thiol group.~~

~~3. The conjugate of claim 2, wherein said thiol group is a cysteine thiol group, optionally wherein said cysteine amino acid residue forms a hinge disulfide bond in an antibody from which the antigen-binding polypeptide is derived (*e.g.*, Cys-226 or Cys-227).~~

~~4. The conjugate of any one of the previous claims, wherein said functionalized group does not conjugate to said scaffold protein.~~

~~5. The conjugate of any one of the previous claims, wherein said scaffold protein is selected from the group consisting of (a) apolipoprotein A, (b) apolipoprotein B, (c) apolipoprotein C, (d) apolipoprotein D, (e) apolipoprotein H, (f) apolipoprotein E, (g) a truncated version of (a)-(f) capable of stabilizing said bilayer, and (h) a combination of any one or more of (a)-(g).~~

~~6. The conjugate of any one of the previous claims, wherein said membrane-forming lipids are selected from the group consisting of C_{4-28} fatty-acyl (*e.g.*, a C_{16} fatty-acyl), DMPC, DOPC, DOPS, DOPE, DPPC, and a combination of any one or more thereof.~~

~~7. The conjugate of any one of the previous claims, wherein one or more of said membrane-forming lipids is a C_{4-28} fatty-acyl and wherein said fatty-acyl is conjugated to a short peptide of 20-60 amino acids.~~

~~8~~2. A conjugate comprising:

a scaffold protein, a membrane-forming lipid, and a short peptide of 20-60 amino acids,

wherein said membrane-forming lipids arrange in a lipid bilayer and said scaffold protein encircles said bilayer; and

wherein said short peptide is conjugated to one or more of said membrane-forming lipids on one or both surfaces of said bilayer.

~~9. The conjugate of claim 8, wherein said membrane-forming lipids are selected from the group consisting of C_{4-28} fatty-acyl (*e.g.*, a C_{16} fatty-acyl), DMPC, DOPC, DOPS, DOPE, DPPC, and a combination of any one or more thereof.~~

~~10. The conjugate of claim 8 or 9, wherein one or more of said membrane-forming lipids is a C_{4-28} fatty-acyl and wherein said fatty-acyl is conjugated to the short peptide of 20-60 amino acids.~~

~~11. The conjugate of claim 7 or 10, wherein said fatty-acyl is a C_{16} fatty-acyl.~~

~~12. The conjugate of any one of claims 7-11, wherein said short peptide is a cystine-knot peptide (CKP).~~

~~13. The conjugate of claim 12 wherein the CKP is EETI-II, circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI-1, SOTI-1, circulin B, cyclopsychotride, or varv peptide A.~~

14. The conjugate of any one of claims 7-11 wherein the short peptide is CKP variant that comprises:

(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;

(b) one or more amino acid insertions, deletions, and/or substitutions at the N terminus relative to a wild type CKP;

(c) one or more amino acid insertions, deletions, and/or substitutions at the C terminus relative to a wild type CKP;

(d) a chemical modification at the N terminus relative to a wild type CKP; and/or

(e) a chemical modification at the C terminus relative to a wild type CKP.

15. The conjugate of claim 14, wherein the CKP variant comprises an additional lysine residue at its N terminus relative to a wild type CKP.

16. The conjugate of claim 14 or 15, wherein the wild type CKP is EETI II.

17. The conjugate of any one of claims 7-16, wherein the activity of the short peptide in the conjugate is higher than the activity of the peptide in a conjugate that does not comprise the antigen binding polypeptide.

18. The conjugate of claim 17, wherein the activity of the peptide in the conjugate is between 2 fold and 10 fold higher than the activity of the peptide in the conjugate that does not comprise the antigen binding polypeptide.

19. The conjugate of claim 15, wherein the activity of the peptide in the conjugate is about 5 fold higher than the activity of the peptide in the conjugate that does not comprise the antigen binding polypeptide.

20. The conjugate of any one of claims 12-16, wherein said short peptide is a CKP or CKP variant having biological activity, wherein 80-90%, 90-95%, or 95-99% of said activity is retained in said conjugate.

21. The conjugate of any one of claims 7-20, wherein said conjugate increases an activity or avidity of said short peptide.

22. The conjugate of any one of claims 7-21, further comprising an antigen-binding polypeptide conjugated to one or more of said membrane-forming lipids on one or both surfaces of said bilayer via a functionalized group on said one or more membrane-forming lipids and a complementary functional group located C-terminally on said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide.

23. The conjugate of any one of claims 7-22, wherein said conjugate comprise 1-100 molecules of said Fab;

optionally wherein said conjugate comprises 5-30, 10-25, 15-20, or 18 molecules of said peptide, and 5-40, 10-35, 15-30, 20-25, or 23 molecules of said antigen binding polypeptide (*e.g.*, Fab); or

optionally wherein said conjugate comprise 3-30, 5-20, 10-15, or 13 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab); or

optionally wherein said conjugate comprise 20-80, 25-70, 30-60, 35-50, or 40 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab).

24. The conjugate of any one of claims 7-23, comprising at least two different peptide C_{4-28} fatty acyl conjugates, wherein a first peptide C_{4-28} fatty acyl conjugate comprises a first short peptide, and wherein a second peptide C_{4-28} fatty acyl comprises a second short peptide that is different from the first short peptide.

25. The conjugate of claim 24, wherein said at least two peptides (*e.g.*, cystine knot peptides) bind different targets, optionally two, three, four, or eight different targets.

26. The conjugate of claim 25, wherein said two or more short peptides bind two different targets.

27. The conjugate of claim 26, wherein said targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.

28. The conjugate of any one of the previous claims, wherein said scaffold protein and said membrane-forming lipids are in a molar ratio of from 1:60 to 1:100, such as 1:80; and/or

wherein 20-35% of said membrane-forming lipids carry the functionalized groups, such as 20%.

29. The conjugate of any one of the previous claims, wherein said antigen binding polypeptide is selected from the group consisting of a Fab, a Fab', a Fab' SH, a $F(ab')_2$, a single chain Fab (scFab), a single chain Fv (scFv), a VH-VH dimer, a VL-VL dimer, a VH-VL dimer, a single domain, a diabody, a linear antibody, and a combination of any one or more thereof, particularly wherein said antigen-binding polypeptide is a Fab;

optionally wherein said Fab binds a target selected from the group consisting of OX40, DR4, GITR, Tie2, factor D, VEGF, MerTK, CD3, Lymphotoxin beta receptor, and a combination of any one or more thereof.

30. The conjugate of any one of the previous claims, wherein said conjugate comprises two or more molecules of said antigen-binding polypeptide, optionally 2-60, 2-32, 10-30, or 20 molecules of said antigen-binding polypeptide.

31. The conjugate of claim 30, wherein said conjugate has 1-160, 10-120, 20-100, 40-80, or 60 molecules of said antigen-binding polypeptide;

wherein said antigen-binding polypeptide is a Fab and said Fab is connected by a PEG spacer to said membrane-forming lipid.

32. The conjugate of claim 31, wherein said PEG spacer connects said functionalized group to said membrane-forming lipid and has a MW of 1000-3000, 1500-2500, 1900-2200, or 2000.

33. The conjugate of any one of claims 30-32, wherein said conjugate increases an activity or avidity of said antigen-binding polypeptide.

34. The conjugate of claim 32, where said activity is OX40 binding and said conjugate has 4-8 molecules of said antigen-binding polypeptide, such as a Fab.

~~35. The conjugate of any one of claims 30-34, wherein said antigen binding polypeptide increases serum stability and/or serum half-life of said conjugate;~~

~~optionally wherein said serum half-life is increased by 2-20 fold, 5-15, or 10-fold.~~

~~36. The conjugate of claim 35, where said conjugate has 5-60, 6-40, or 7-32 molecules of said antigen binding polypeptide.~~

~~37. The conjugate of any one of claims 30-36 wherein said two or more antigen binding polypeptides bind different targets or epitopes, optionally two, three, four, or eight different targets or epitopes.~~

~~38. The conjugate of claim 37, wherein said two or more antigen-binding polypeptides bind two different targets or epitopes.~~

~~39. The conjugate of claim 37, wherein said targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.~~

~~40. The conjugate of any one of the preceding claims, wherein the antigen binding polypeptide is a Fab or a Fab-like molecule, optionally a human or humanized Fab.~~

~~41. The conjugate of any one of the preceding claims, wherein the spacer comprises PEG or the amino acid sequence of GSGS.~~

~~42~~3. A pharmaceutical composition comprising the conjugate of any one of the previous claims and a pharmaceutically acceptable vehicle.

~~43. The pharmaceutical composition of claim 42, wherein said composition is a liquid composition having a viscosity of 10-50 cP and a concentration of 100-300 mg of said conjugate/mL.~~

~~44. The conjugate of any one of claims 1-41 or the pharmaceutical composition of claim 42 or 43, wherein said conjugate or composition is administered subcutaneously or via ocular delivery.~~

~~45. The conjugate or the pharmaceutical composition of claim 44, wherein said conjugate or composition is lyophilized, such as in the presence of trehalose; and optionally reconstituted.~~

~~46. The conjugate or pharmaceutical composition of claim 45, wherein said conjugate comprises 18-20 Fab molecules per conjugate; and/or~~

~~wherein lyophilization occurs in the presence of 80 mM trehalose; and/or~~

~~wherein lyophilization occurs at a concentration of 5 mg conjugate/mL.~~

~~47. The conjugate or pharmaceutical composition of claim 45 or 46, wherein 80-90%, 90-95%, or 95-99% of antigen binding activity of said antigen binding polypeptide is retained following lyophilization and reconstitution.~~

~~48~~4. A liquid formulation comprising 100-300 mg of the conjugate of ~~any one of claims 1-41~~ claim 1 or 2 and having a viscosity of 10-50 cP, optionally wherein said formulation is ~~administered~~ for administration subcutaneously or via ocular delivery.

~~49~~5. A method of preparing a conjugate of a nanolipoprotein particle and an antigen-binding polypeptide, comprising:

a) providing a scaffold protein and a membrane-forming lipid under conditions allowing (self-)assembly of a nanolipoprotein particle comprising a lipid bilayer of said membrane-forming lipids encircled by said scaffold protein, wherein one or more of said membrane-forming lipids presents a functionalized group on one or both surfaces of said particle;

b) allowing said particle to contact an antigen-binding polypeptide (*e.g.*, a Fab) having a C-terminally located complementary functional group that conjugates to said functionalized group at low pH in the range of 4.5 to 6.5 pH; and

c) optionally purifying the conjugate of said particle and said antigen-binding polypeptide.

~~50. The method of claim 49, wherein said step b) follows said step a) without an intervening step to remove some or all unassembled membrane-forming lipids.~~

~~51. The method of claim 49 or 50, wherein said functionalized group is a maleimide derivative and wherein said functional group is a cysteine thiol group, optionally wherein said cysteine amino acid residue forms a hinge disulfide bond in the antibody from which the antigen binding polypeptide is derived (such as Cys-226 or Cys-227).~~

~~52. The method of any one of claims 49-51, wherein said functionalized group does not conjugate to said scaffold protein at said low pH.~~

~~53. The method of claim 52, wherein said low pH is a pH of 5.5 to 6.5, a pH of 5-6, or a pH of 6.~~

~~54. The method of any one of claims 49-53, wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide.~~

~~55. The method of claim 54, wherein said spacer is a PEG spacer that connects said functionalized group to said membrane-forming lipid.~~

~~56. The method of claim 55, wherein said PEG spacer has a MW of 1000-3000, 1500-2500, 1900-2200, or 2000.~~

~~57. The method of any one of claims 49-56, wherein one or more of said membrane-forming lipids is a C_{4-28} fatty-acyl and wherein said fatty-acyl is conjugated to a short peptide of 20-60 amino acids.~~

~~58. The method of claim 57, wherein said fatty-acyl is a C_{16} fatty-acyl.~~

~~59. The method of claim 57 or 58, wherein said short peptide is a cystine-knot peptide (CKP).~~

60. The method of claim 59, wherein the CKP is EETI-II, circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI-1, SOTI-1, circulin B, cyclopsychotride, or varv peptide A.

61. The method of claim 57 or 58, wherein the short peptide is CKP variant that comprises:

(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;

(b) one or more amino acid insertions, deletions, and/or substitutions at the N terminus relative to a wild type CKP;

(c) one or more amino acid insertions, deletions, and/or substitutions at the C-terminus relative to a wild type CKP;

(d) a chemical modification at the N-terminus relative to a wild type CKP; and/or

(e) a chemical modification at the C-terminus relative to a wild type CKP.

62. The method of claim 61, wherein the CKP variant comprises an additional lysine residue at its N-terminus relative to a wild type CKP.

63. The method of claim 61 or 62, wherein the wild type CKP is EETI-II.

64. The method of any one of claims 57-63, wherein said membrane forming lipids comprise a peptide C_{4-28} fatty acyl conjugate and at least one more of DMPC, DOPC, DOPS, DOPE, DPPC (*e.g.*, a peptide C_{16} fatty acyl conjugate and DOPC) in the molar ratio of 1:3 to 1:15, or 1:6 to 1:12, or 1:9; and/or wherein said conjugate comprises 1-100, 10-90, 20-80, 30-70, 40-60, or 60 molecules of said short peptide.

65. The method of any one of claims 57-64, wherein the activity of the short peptide in the conjugate is higher than the activity of the peptide in a conjugate that does not comprise the antigen-binding polypeptide.

66. The method of claim 65, wherein the activity of the peptide in the conjugate is between 2-fold and 10-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.

67. The method of claim 66, wherein the activity of the peptide in the conjugate is about 5-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.

68. The method of any one of claims 57-64, wherein said short peptide is a CKP or CKP variant having biological activity, wherein 80-90%, 90-95%, or 95-99% of said activity is retained in said conjugate.

69. The method of any one of claims 57-68, wherein said conjugate comprise 1-100 molecules of said Fab;

optionally wherein said conjugate comprises 5-30, 10-25, 15-20, or 18 molecules of said peptide, and 5-40, 10-35, 15-30, 20-25, or 23 molecules of said antigen binding polypeptide (*e.g.*, Fab); or

optionally wherein said conjugate comprise 3-30, 5-20, 10-15, or 13 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab); or optionally wherein said conjugate comprise 20-80, 25-70, 30-60, 35-50, or 40 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab).

70. The method of claim 69, wherein the Fab and the short peptide bind two different targets.

71. The method of any one of claims 57-70, comprising at least two different peptide C_{4-28} fatty acyl conjugates, wherein a first peptide C_{4-28} fatty acyl conjugate comprises a first short peptide, and wherein a second peptide C_{4-28} fatty acyl comprises a second short peptide that is different from the first short peptide.

72. The method of claim 71, wherein said at least two peptides (*e.g.*, cystine knot peptides) bind different targets, optionally two, three, four, or eight different targets.

73. The method of claim 72, wherein said two or more short peptides bind two different targets.

~~74. The method of claim 70 or 73, wherein said targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.~~

~~75~~6. A method of preparing a conjugate of a nanolipoprotein particle and a short peptide of 20-60 amino acids (*e.g.*, a cystine-knot peptide), comprising:

a) providing a scaffold protein and a membrane-forming lipid under conditions allowing (self-)assembly of a nanolipoprotein particle comprising a lipid bilayer of said membrane-forming lipids encircled by said scaffold protein;

wherein one or more of said membrane-forming lipids comprises a C_{4-28} fatty-acyl (*e.g.*, a C_{16} fatty-acyl) and fatty-acyl is conjugated to said short peptide; and

optionally purifying the peptide conjugate.

~~76. The method of claim 75, wherein said short peptide is a cystine-knot peptide (CKP).~~

~~77. The method of claim 76, wherein the CKP is EETI II, circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI-1, SOTI-1, circulin B, cyclopsychotride, or varv peptide A.~~

~~78. The method of claim 77, wherein the short peptide is CKP variant that comprises:~~

~~(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;~~

~~(b) one or more amino acid insertions, deletions, and/or substitutions at the N-terminus relative to a wild type CKP;~~

~~(c) one or more amino acid insertions, deletions, and/or substitutions at the C-terminus relative to a wild type CKP;~~

~~(d) a chemical modification at the N-terminus relative to a wild type CKP; and/or~~

~~(e) a chemical modification at the C-terminus relative to a wild type CKP.~~

~~79. The method of claim 78, wherein the CKP variant comprises an additional lysine residue at its N-terminus relative to a wild type CKP.~~

~~80. The method of claim 78 or 79, wherein the wild type CKP is EETI-II.~~

81. The method of any one of claims 75-80, wherein said membrane forming lipids comprise a peptide-C_{4-28} fatty-acyl conjugate and at least one more of DMPC, DOPC, DOPS, DOPE, DPPC (*e.g.*, a peptide-C_{16} fatty-acyl conjugate and DOPC) in the molar ratio of 1:3 to 1:15, or 1:6 to 1:12, or 1:9; and/or wherein said conjugate comprises 1-100, 10-90, 20-80, 30-70, 40-60, or 60 molecules of said short peptide.

82. The method of any one of claims 75-81, comprising at least two different peptide-C_{4-28} fatty-acyl conjugates, wherein a first peptide-C_{4-28} fatty-acyl conjugate comprises a first short peptide, and wherein a second peptide-C_{4-28} fatty-acyl comprises a second short peptide that is different from the first short peptide.

83. The method of claim 82, wherein said at least two peptides (*e.g.*, cystine-knot peptides) bind different targets, optionally two, three, four, or eight different targets.

84. The method of claim 82, wherein said two or more short peptides bind two different targets.

85. The method of claim 84, wherein said targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.

86. The method of any one of claims 75-85, wherein said short peptide is a CKP or CKP variant having biological activity, wherein 80-90%, 90-95%, or 95-99% of said activity is retained in said conjugate.

87. The method any one of claims 75-86, wherein one or more of said membrane forming lipids presents a functionalized group on one or both surfaces of said particle; and further comprising the step of:

b) allowing said particle to contact an antigen binding polypeptide (*e.g.*, a Fab) having a C-terminally located complementary functional group that conjugates to said functionalized group at low pH in the range of 4.5 to 6.5 pH;

wherein said step b) follows said step a) without an intervening step to remove some or all unassembled membrane forming lipids; and/or without an intervening step to enrich the peptide conjugate of step a).

88. The method of claim 87, wherein said functionalized group is a maleimide derivative and wherein said functional group is a cysteine thiol group, optionally wherein said cysteine amino acid residue forms a hinge disulfide bond in the antibody from which the antigen-binding polypeptide is derived (such as Cys-226 or Cys-227).

89. The method of claim 87 or 88, wherein said functionalized group does not conjugate to said scaffold protein at said low pH.

90. The method of claim 89 wherein said low pH is a pH of 5.5 to 6.5, a pH of 5-6, or a pH of 6.

91. The method of any one of claims 87-90, wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide.

92. The method of claim 91, wherein said spacer is a PEG spacer that connects said functionalized group to said membrane-forming lipid.

93. The method of claim 92, wherein said PEG spacer has a MW of 1000-3000, 1500-2500, 1900-2200, or 2000.

94. The method of any one of claims 87-93, wherein said conjugate increases an activity or avidity of said short peptide.

95. The method of any one of claims 87-94, wherein said conjugate comprise 1-100 molecules of said Fab;

optionally wherein said conjugate comprises 5-30, 10-25, 15-20, or 18 molecules of said peptide, and 5-40, 10-35, 15-30, 20-25, or 23 molecules of said antigen binding polypeptide (*e.g.*, Fab); or

optionally wherein said conjugate comprise 3-30, 5-20, 10-15, or 13 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab); or optionally wherein said conjugate comprise 20-80, 25-70, 30-60, 35-50, or 40 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab).

~~96. The method of claim 95, wherein the Fab and the short peptide bind two different targets.~~

~~97. The method of claim 96, wherein said targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.~~

~~98. The method of any one of claims 87-97, wherein the activity of the short peptide in the conjugate is higher than the activity of the peptide in a conjugate that does not comprise the antigen-binding polypeptide.~~

~~99. The method of claim 98, wherein the activity of the peptide in the conjugate is between 2-fold and 10-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.~~

~~100. The method of claim 99, wherein the activity of the peptide in the conjugate is about 5-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.~~

~~101~~7. A conjugate produced by the method of ~~any one of claims 49-100~~claim 5 or 6.

~~102~~8. A method of increasing avidity, activity, and/or potency of an antigen-binding polypeptide, said method comprising:

a) providing a scaffold protein and a membrane-forming lipid under conditions allowing (self-)assembly of a nanolipoprotein particle comprising a lipid bilayer of said membrane-forming lipids encircled by said scaffold protein, wherein one or more of said membrane-forming lipids presents a functionalized group on one or both surfaces of said particle;

b) allowing said particle to contact an antigen-binding polypeptide (*e.g.*, a Fab) having a C-terminally located complementary functional group that conjugates to said functionalized group at low pH in the range of 4.5 to 6.5 pH; and

c) optionally purifying the conjugate of said particle and said antigen-binding polypeptide,

thereby increasing avidity, activity, and/or potency of said antigen-binding polypeptide.

~~103. The method of claim 102, wherein said antigen-binding polypeptide is a Fab or a Fab-like molecule and/or wherein said conjugate comprises 10-60, 15-30, or 20 molecules of said antigen-binding polypeptides.~~

~~104. The method of claim 103, wherein said antigen-binding polypeptide is a Fab or a Fab-like molecule connected by a PEG spacer to said membrane-forming lipid; and~~

~~wherein said conjugate comprises 1-160, 10-120, 20-100, 40-80, or 60 molecules of said antigen-binding polypeptides.~~

~~105. The method of claim 104, wherein said PEG spacer connects said functionalized group to said membrane-forming lipid and has a MW of 1000-3000, 1500-2500, 1900-2200, or 2000.~~

~~106. The method of any one of claims 102-105, wherein said conjugate is stabilized,~~

~~optionally wherein said conjugate comprises 7-60, 7-32, 40-60, or 50 molecules of said antigen-binding polypeptides.~~

~~107. The method of any one of claims 102-106, wherein said conjugate further comprises one or more molecules of a second antigen-binding polypeptide that binds a different target.~~

~~108. The method of any one of claims 102-107, wherein said conjugate is provided in a liquid formulation, said formulation comprising 100-300 mg of said conjugate and having a viscosity of 10-50 cP.~~

~~109. The method of any one of claims 102-108, wherein one or more of said membrane-forming lipids is a C_{4-28} fatty acyl and wherein said fatty acyl is conjugated to a short peptide of 20-60 amino acids, and wherein the method increases the avidity, activity, and/or potency of the short peptide.~~

~~110. The method of claim 109, wherein said fatty acyl is a C_{16} fatty acyl.~~

111. The method of claim 109 or 110, wherein said short peptide is a cystine knot peptide (CKP).

112. The method of claim 111, wherein the CKP is EETI II I, circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI 1, SOTI 1, circulin B, cyclopsychotride, or varv peptide A.

113. The method of claim 109 or 110, wherein the short peptide is CKP variant that comprises:

(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;

(b) one or more amino acid insertions, deletions, and/or substitutions at the N terminus relative to a wild type CKP;

(c) one or more amino acid insertions, deletions, and/or substitutions at the C terminus relative to a wild type CKP;

(d) a chemical modification at the N terminus relative to a wild type CKP; and/or

(e) a chemical modification at the C terminus relative to a wild type CKP.

114. The method of claim 113, wherein the CKP variant comprises an additional lysine residue at its N terminus relative to a wild type CKP.

115. The method of claim 113 or 114, wherein the wild type CKP is EETI II.

116. The method of any one of claims 109-115, wherein said membrane forming lipids comprise a peptide-C_{4-28} fatty-acyl conjugate and at least one more of DMPC, DOPC, DOPS, DOPE, DPPC (*e.g.*, a peptide C_{16} fatty acyl conjugate and DOPC) in the molar ratio of 1:3 to 1:15, or 1:6 to 1:12, or 1:9; and/or wherein said conjugate comprises 1-100, 10-90, 20-80, 30-70, 40-60, or 60 molecules of said short peptide.

117. The method of any one of claims 109-116, comprising at least two different peptide-C_{4-28} fatty acyl conjugates, wherein a first peptide-C_{4-28} fatty acyl conjugate comprises a first short peptide, and wherein a second peptide-C_{4-28} fatty acyl comprises a second short peptide that is different from the first short peptide.

~~118. The method of claim 117, wherein said at least two peptides (*e.g.*, cystine knot peptides) bind different targets, optionally two, three, four, or eight different targets.~~

~~119. The method of claim 118, wherein said two or more short peptides bind two different targets.~~

~~120. The method of claim 119, wherein said targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.~~

~~121. The method of any one of claims 109-120, wherein said conjugate comprise 1-100 molecules of said Fab;~~

~~optionally wherein said conjugate comprises 5-30, 10-25, 15-20, or 18 molecules of said peptide, and 5-40, 10-35, 15-30, 20-25, or 23 molecules of said antigen binding polypeptide (*e.g.*, Fab); or~~

~~optionally wherein said conjugate comprise 3-30, 5-20, 10-15, or 13 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab); or optionally wherein said conjugate comprise 20-80, 25-70, 30-60, 35-50, or 40 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab).~~

~~122. The method of any one of claims 110-121, wherein the activity of the short peptide in the conjugate is higher than the activity of the peptide in a conjugate that does not comprise the antigen-binding polypeptide.~~

~~123. The method of claim 122, wherein the activity of the peptide in the conjugate is between 2-fold and 10-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.~~

~~124. The method of claim 123, wherein the activity of the peptide in the conjugate is about 5-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.~~

~~125~~9. A method of increasing stability, shelf-life, and/or half-life of an antigen-binding polypeptide, said method comprising:

a) providing a scaffold protein and a membrane-forming lipid under conditions allowing (self-)assembly of a nanolipoprotein particle comprising a lipid bilayer of said membrane-forming lipids encircled by said scaffold protein, wherein one or more of said membrane-forming lipids presents a functionalized group on one or both surfaces of said particle;

b) allowing said particle to contact an antigen-binding polypeptide (*e.g.*, a Fab) having a C-terminally located complementary functional group that conjugates to said functionalized group at low pH in the range of 4.5 to 6.5 pH; and

c) optionally purifying the conjugate of said particle and said antigen-binding polypeptide,

thereby increasing stability, shelf-life, and/or half-life of said antigen-binding polypeptide.

~~126~~10. A method of increasing stability, shelf-life, and/or half-life of a nanolipoprotein particle, said method comprising

a) providing a scaffold protein and a membrane-forming lipid under conditions allowing (self-)assembly of a nanolipoprotein particle comprising a lipid bilayer of said membrane-forming lipids encircled by said scaffold protein, wherein one or more of said membrane-forming lipids presents a functionalized group on one or both surfaces of said particle;

b) allowing said particle to contact an antigen-binding polypeptide (*e.g.*, a Fab) having a C-terminally located complementary functional group that conjugates to said functionalized group at low pH in the range of 4.5 to 6.5 pH; and

c) optionally purifying the conjugate of said particle and said antigen-binding polypeptide,

thereby increasing stability, shelf-life, and/or half-life of said nanolipoprotein particle.

~~127. The method of claim 125 or 126, wherein one or more of said membrane forming lipids is a C_{4-28} fatty acyl and wherein said fatty acyl is conjugated to a short peptide of 20-60 amino acids.~~

~~128. The method of claim 127, wherein said fatty acyl is a C_{16} fatty acyl.~~

~~129~~11. A method of increasing the stability, shelf-life, and/or half-life of a short peptide that is 20-60 amino acids in length, said method comprising:

a) providing a scaffold protein and a membrane-forming lipid under conditions allowing (self-)assembly of a nanolipoprotein particle comprising a lipid bilayer of said membrane-forming lipids encircled by said scaffold protein;

wherein one or more of said membrane-forming lipids comprises a C_{4-28} fatty-acyl (*e.g.*, a C_{16} fatty-acyl) and fatty-acyl is conjugated to said short peptide; and

optionally purifying the peptide conjugate;

b) modifying one or more of said membrane-forming lipids to a present functionalized group on one or both surfaces of said particle, and

c) allowing said particle to contact an antigen-binding polypeptide (*e.g.*, a Fab) having a C-terminally located complementary functional group that conjugates to said functionalized group at low pH in the range of 4.5 to 6.5 pH;

wherein said step c) follows said step b) without an intervening step to remove some or all unassembled membrane-forming lipids; and/or without an intervening step to enrich the peptide conjugate of step b)

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide,

thereby increasing stability, shelf-life, and/or half-life of said short peptide.

~~130. The method of any one of claims 127-129, wherein said fatty-acyl is a C_{16} fatty-acyl.~~

~~131. The method any one of claims 127-130, wherein said short peptide is a cystine knot peptide (CKP).~~

~~132. The method of claim 131, wherein the CKP is EETI-II-I, circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI-1, SOTI-1, circulin B, cyclopsychotride, or varv peptide A.~~

~~133. The method of any one of claims 127-130, wherein the short peptide is CKP variant that comprises:~~

~~(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;~~

(b) one or more amino acid insertions, deletions, and/or substitutions at the N-terminus relative to a wild type CKP;

(c) one or more amino acid insertions, deletions, and/or substitutions at the C-terminus relative to a wild type CKP;

(d) a chemical modification at the N-terminus relative to a wild type CKP; and/or

(e) a chemical modification at the C-terminus relative to a wild type CKP.

134. The method of claim 133, wherein the CKP variant comprises an additional lysine residue at its N-terminus relative to a wild type CKP.

135. The method of claim 133 or 134 wherein the wild type CKP is EETI II.

136. The method of any one of claims 127-135, wherein said membrane forming lipids comprise a peptide C_{4-28} fatty acyl conjugate and at least one more of DMPC, DOPC, DOPS, DOPE, DPPC (*e.g.*, a peptide C_{16} fatty acyl conjugate and DOPC) in the molar ratio of 1:3 to 1:15, or 1:6 to 1:12, or 1:9; and/or wherein said conjugate comprises 1-100, 10-90, 20-80, 30-70, 40-60, or 60 molecules of said short peptide.

137. The method of any one of claims 125-136, wherein said antigen binding polypeptide is a Fab or a Fab-like molecule and/or wherein said conjugate comprises 5-60, 6-40, 7-32, 40-60, or 50 molecules of said antigen binding polypeptides (*e.g.*, said Fab).

138. The conjugate of any one of claims 127-136, wherein said conjugate comprise 1-100 molecules of said Fab;

optionally wherein said conjugate comprises 5-30, 10-25, 15-20, or 18 molecules of said peptide, and 5-40, 10-35, 15-30, 20-25, or 23 molecules of said antigen binding polypeptide (*e.g.*, Fab); or

optionally wherein said conjugate comprise 3-30, 5-20, 10-15, or 13 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab); or optionally wherein said conjugate comprise 20-80, 25-70, 30-60, 35-50, or 40 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab).

139. The method of any one of claims 125-138, wherein said conjugate further comprises a biologically active agent or a detectable agent,

~~optionally wherein said biologically active agent is a cytotoxic agent selected from the group consisting of daunomycin, doxorubicin, methotrexate, vindesine, a radionuclide, diphtheria toxin, ricin, geldanamycin, a maytansinoid, calicheamicin, and a combination of any one or more thereof; and/or~~

~~optionally wherein said detectable agent is at least one label selected from the group consisting a radioactive isotope, a fluorophore, a chemiluminescent dye, a chromophore, an enzyme, a metal ion, a nanoparticle, and a combination of any one or more thereof.~~

~~140. The method of any one of claims 125-139, wherein said conjugate is provided in a liquid formulation, said formulation comprising 100-300 mg of said conjugate and having a viscosity of 10-50 cP.~~

~~141~~12. The conjugate of any one of claims 1-~~41~~2 and ~~101~~7, or the ~~conjugate or~~ pharmaceutical composition of ~~any one of claims 42-47~~claim 3, or the formulation of claim ~~48~~4, for use as a medicament.

~~142. The conjugate of any one of claims 1-41 and 101, or the conjugate or pharmaceutical composition of any one of claims 42-47, or the formulation of claim 48, for use in treating cancer or ocular disorders.~~

~~143~~13. Use of the conjugate of any one of claims 1-~~41~~2 and ~~101~~7, or the ~~conjugate or~~ pharmaceutical composition of ~~any one of claims 42-47~~claim 3, or the formulation of claim ~~48~~4, in the manufacture of a medicament for treatment of cancer or ocular disorders.

~~144~~14. Use of the conjugate of any one of claims 1-~~41~~2 and ~~101~~7, or the ~~conjugate or~~ pharmaceutical composition of ~~any one of claims 42-47~~claim 3, or the formulation of claim ~~48~~4, in the manufacture of a medicament for inhibiting angiogenesis and/or tumor growth.

~~145~~15. The conjugate of any one of claims 1-2 and 7, or the pharmaceutical composition of claim 3, or the formulation of claim 4, for use in ~~A method of~~ treating an individual with an antigen-binding polypeptide (*e.g.*, a Fab)~~, comprising administering to the individual an effective amount of the conjugate of any one of claims 1-41 and 101, or the conjugate or pharmaceutical composition of any one of claims 42-47, or the formulation of claim 48;~~

optionally wherein said conjugate, pharmaceutical composition or formulation is for administration with ~~further comprising administering~~ an additional therapeutic agent ~~to the individual~~.

~~146~~16. The conjugate of any one of claims 1-2 and 7, or the pharmaceutical composition of claim 3, or the formulation of claim 4, for use in ~~A method of~~ delivering an antigen-binding polypeptide (*e.g.*, a Fab) to an individual in need thereof, ~~said method comprising~~

~~providing the conjugate of any one of claims 1-41 and 101, or the conjugate or pharmaceutical composition of any one of claims 42-47, or the formulation of claim 48; and~~

~~administering~~ wherein said conjugate, composition, or formulation is to be administered to said individual,

thereby delivering said antigen-binding polypeptide to said individual.

~~147~~17. A liquid formulation comprising a conjugate of an antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle, for use in ~~A method of~~ delivering an antigen-binding polypeptide (*e.g.*, a Fab) to an individual in need thereof, in a potent, stable liquid formulation, ~~said method comprising:~~

~~administering~~ wherein said liquid formulation is to be administered to ~~an~~ said individual ~~a liquid formulation comprising a conjugate of said antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle~~;

wherein said nanolipoprotein particle comprises a scaffold protein encircling a bilipid layer of membrane-forming lipids;

wherein said membrane-forming lipids are conjugated to 5-100 molecules of said antigen-binding polypeptide via a functionalized group on said membrane-forming lipid and a C-terminally located complementary functional group on said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide,

thereby delivering said antigen-binding polypeptide to ~~an~~ said individual in a stable liquid formulation.

~~148~~18. A liquid formulation comprising a conjugate of an antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle, for use in ~~A method of~~ delivering an antigen-binding polypeptide (*e.g.*, a Fab) to an individual in need thereof, in a potent, low viscosity formulation, ~~said method comprising:~~

~~administering~~ wherein said liquid formulation is to be administered to ~~an~~ said individual ~~a liquid formulation comprising a conjugate of said antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle~~;

wherein said nanolipoprotein particle comprises a scaffold protein encircling a bilipid layer of membrane-forming lipids;

wherein one or more of said membrane-forming lipids is conjugated to said antigen-binding polypeptide via a functionalized group on said one or more membrane-forming lipids and a C-terminally located complementary functional group on said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide; and

wherein said liquid formulation has a viscosity of 10-50 cP and a concentration of 100-300 mg of said conjugate/mL,

thereby delivering said antigen-binding polypeptide to ~~an~~ said individual in a low viscosity formulation.

~~149. The method of claim 147 or 148, wherein one or more of said membrane-forming lipids is a C_{4-28} fatty acyl and wherein said fatty acyl is conjugated to a short peptide of 20-60 amino acids.~~

~~150~~19. A liquid formulation comprising a conjugate of an antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle, for use in ~~A method of~~ delivering a short peptide 20-60 amino acids in length to an individual in need thereof, in a potent, stable liquid formulation, ~~said method comprising:~~

~~administering~~ wherein said liquid formulation is to be administered to ~~an~~ said individual ~~a liquid formulation comprising a conjugate of said antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle~~;

wherein said nanolipoprotein particle comprises a scaffold protein encircling a bilipid layer of membrane-forming lipids;

wherein one or more of said membrane-forming lipids is a C_{4-28} fatty-acyl and wherein said fatty-acyl is conjugated to a short peptide of 20-60 amino acids;

wherein said membrane-forming lipids are conjugated to 5-100 molecules of said antigen-binding polypeptide via a functionalized group on said membrane-forming lipid and a C-terminally located complementary functional group on said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide,

thereby delivering said short peptide ~~antigen-binding polypeptide~~ to ~~an~~ said individual in a stable liquid formulation.

~~151~~20. A liquid formulation comprising a conjugate of an antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle, for use in ~~A method of~~ delivering a short peptide 20-60 amino acids in length to an individual in need thereof, in a potent, low viscosity formulation, ~~said method comprising:~~

~~administering~~ wherein said liquid formulation is to be administered to ~~an~~ said individual ~~a liquid formulation comprising a conjugate of said antigen-binding polypeptide (*e.g.*, said Fab) and a nanolipoprotein particle~~;

wherein said nanolipoprotein particle comprises a scaffold protein encircling a bilipid layer of membrane-forming lipids;

wherein one or more of said membrane-forming lipids is a C_{4-28} fatty-acyl and wherein said fatty-acyl is conjugated to a short peptide of 20-60 amino acids;

wherein one or more of said membrane-forming lipids is conjugated to said antigen-binding polypeptide via a functionalized group on said one or more membrane-forming lipids and a C-terminally located complementary functional group on said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide; and

wherein said liquid formulation has a viscosity of 10-50 cP and a concentration of 100-300 mg of said conjugate/mL,

thereby delivering said short peptide ~~antigen-binding polypeptide~~ to ~~an~~ said individual in a low viscosity formulation.

~~152. The method of any one of claims 149-151, wherein said fatty-acyl is a C_{16} fatty-acyl.~~

~~153. The method any one of claims 149-152, wherein said short peptide is a cystine knot peptide (CKP).~~

~~154. The method of claim 153, wherein the CKP is EETI-II , circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI-1, SOTI-1, circulin B, cyclopsychotride, or varv peptide A.~~

~~155. The method of claim 149-152, wherein the short peptide is CKP variant that comprises:~~

~~(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;~~

~~(b) one or more amino acid insertions, deletions, and/or substitutions at the N-terminus relative to a wild type CKP;~~

~~(c) one or more amino acid insertions, deletions, and/or substitutions at the C-terminus relative to a wild type CKP;~~

~~(d) a chemical modification at the N-terminus relative to a wild type CKP; and/or~~

~~(e) a chemical modification at the C-terminus relative to a wild type CKP.~~

~~156. The method of claim 155, wherein the CKP variant comprises an additional lysine residue at its N-terminus relative to a wild type CKP.~~

~~157. The method of claim 155 or 156, wherein the wild type CKP is EETI-II.~~

~~158. The method of any one of claims 149-157, wherein said membrane forming lipids comprise a peptide-C_{4-28} fatty-acyl conjugate and at least one more of DMPC, DOPC, DOPS, DOPE, DPPC (*e.g.*, a peptide-C_{16} fatty-acyl conjugate and DOPC) in the molar ratio of 1:3 to 1:15, or 1:6 to 1:12, or 1:9; and/or wherein said conjugate comprises 1-100, 10-90, 20-80, 30-70, 40-60, or 60 molecules of said short peptide.~~

~~159. The method of any one of claims 149-158, wherein the activity of the short peptide in the conjugate is higher than the activity of the peptide in a conjugate that does not comprise the antigen-binding polypeptide.~~

~~160. The method of claim 159, wherein the activity of the peptide in the conjugate is between 2-fold and 10-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.~~

~~161. The method of claim 160, wherein the activity of the peptide in the conjugate is about 5-fold higher than the activity of the peptide in the conjugate that does not comprise the antigen-binding polypeptide.~~

~~162. The method of any one of claims 149-161, wherein said conjugate comprise 1-100 molecules of said Fab;~~

~~optionally wherein said conjugate comprises 5-30, 10-25, 15-20, or 18 molecules of said peptide, and 5-40, 10-35, 15-30, 20-25, or 23 molecules of said antigen binding polypeptide (*e.g.*, Fab); or~~

~~optionally wherein said conjugate comprise 3-30, 5-20, 10-15, or 13 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab); or optionally wherein said conjugate comprise 20-80, 25-70, 30-60, 35-50, or 40 molecules of said peptide and 10-60 molecules of said antigen binding polypeptide (*e.g.*, Fab).~~

~~163. The method of any one of claims 147-162, wherein said spacer is a PEG spacer that connects said functionalized group to said membrane-forming lipid.~~

~~164. The method of claim 163, wherein said PEG spacer has a MW of 1000-3000, 1500-2500, 1900-2200, or 2000.~~

~~165. The method any one of claims 149-164, wherein said antigen-binding polypeptide (*e.g.*, a Fab) and said short peptide each bind the same target.~~

~~166. The method any one of claims 149-164, wherein said antigen-binding polypeptide (*e.g.*, a Fab) and said short peptide each bind a different target.~~

~~167. The method of any one of claims 147-166, wherein said antigen-binding polypeptide is a Fab that binds a target selected from the group consisting of factor D, VEGF, Tie2,~~

~~DR4; and a combination of any one or more thereof; and said formulation is administered via ocular delivery.~~

~~168. The method of any one of claims 149-167, wherein said short peptide binds a target selected from the group consisting of factor D, VEGF, Tie2, DR4, and a combination of any one or more thereof.~~

~~169. The method of any one of claims 147-166, wherein said antigen binding polypeptide is a Fab that binds a target selected from the group consisting of OX40, DR4, GITR, Tie2, factor D, VEGF, MerTK, CD3, Lymphotoxin beta receptor, and a combination of any one or more thereof.~~

~~170. The method of any one of claims 150-166 and 169, wherein said short peptide binds a target selected from the group consisting of OX40, DR4, GITR, Tie2, factor D, VEGF, MerTK, CD3, Lymphotoxin beta receptor, and a combination of any one or more thereof.~~

~~171. The method of any one of claims 147-166, wherein said antigen binding polypeptides bind at least two different targets.~~

~~172. The method of claim 171, wherein said two different targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.~~

~~173. The method of any one of claims 149-164, wherein said short peptide and said antigen-binding polypeptide bind at least two different targets.~~

~~174. The method of claim 173, wherein said two different targets are a pair selected from the group consisting of CD3 and CD19; CD3 and EpCAM; CD3 and CEA; CD16 and CD30; CD16 and CD33; Ang-2 and VEGF-A; and Factor X and Factor IXa.~~

~~175~~21. A liquid formulation comprising a conjugate of an antigen-binding polypeptide (*e.g.*, a Fab), a nanolipoprotein particle, and a biologically active agent or a detectable agent,

for use in ~~A method of~~ delivering a biologically active agent or a detectable agent to an individual in need thereof, in a stable liquid formulation, ~~said method comprising:~~

~~administering~~ wherein said liquid formulation is to be administered to ~~an~~ said individual ~~a liquid formulation comprising a conjugate of an antigen binding polypeptide (*e.g.*, a Fab), a nanolipoprotein particle, and a biologically active agent or a detectable agent~~,

wherein said nanolipoprotein particle comprises a scaffold protein encircling a bilipid layer of membrane-forming lipids;

wherein said membrane-forming lipids are conjugated to 5-100 molecules of said antigen-binding polypeptide via a functionalized group on said membrane-forming lipid and a C-terminally located complementary functional group on said antigen-binding polypeptide;

wherein said biologically active agent or said detectable agent is conjugated to at least one of said scaffold protein, said membrane-forming lipid, or said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide,

thereby delivering said biologically active agent or said detectable agent to ~~an~~ said individual in need thereof in a stable liquid formulation.

~~176~~22. A liquid formulation comprising a conjugate of an antigen-binding polypeptide (*e.g.*, a Fab), a nanolipoprotein particle, and a biologically active agent or a detectable agent, for use in ~~A method of~~ delivering a biologically active agent or a detectable agent to an individual in need thereof, in a low viscosity formulation, ~~said method comprising:~~

~~administering~~ wherein said liquid formulation is to be administered to ~~an~~ said individual ~~a liquid formulation comprising a conjugate of an antigen binding polypeptide (*e.g.*, a Fab), a nanolipoprotein particle, and a biologically active agent or a detectable agent~~,

wherein said nanolipoprotein particle comprises a scaffold protein encircling a bilipid layer of membrane-forming lipids;

wherein one or more of said membrane-forming lipids is conjugated to said antigen-binding polypeptide via a functionalized group on said one or more membrane-

forming lipids and a C-terminally located complementary functional group on said antigen-binding polypeptide;

wherein said biologically active agent or said detectable agent is conjugated to at least one of said scaffold protein, said membrane-forming lipid, or said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide; and

wherein said liquid formulation has a viscosity of 10-50 cP and a concentration of 100-300 mg of said conjugate/mL,

thereby delivering said biologically active agent or said detectable agent to ~~an~~ said individual in need thereof in a low viscosity formulation.

~~177~~23. A liquid formulation comprising a conjugate of an antigen-binding polypeptide (*e.g.*, a Fab), a nanolipoprotein particle, and a biologically active agent or a detectable agent, for use in ~~A method of~~ delivering a biologically active agent or a detectable agent to the brain or central nervous system of an individual in need thereof, ~~said method comprising:~~

~~systemically administering to an individual a~~wherein said liquid formulation is for administration systemically ~~comprising a conjugate of an antigen-binding polypeptide (*e.g.*, a Fab), a nanolipoprotein particle, and a biologically active agent or a detectable agent~~,

wherein said nanolipoprotein particle comprises a scaffold protein encircling a bilipid layer of membrane-forming lipids;

wherein one or more of said membrane-forming lipids is conjugated to said antigen-binding polypeptide via a functionalized group on said one or more membrane-forming lipids and a C-terminally located complementary functional group on said antigen-binding polypeptide;

wherein said biologically active agent or said detectable agent is conjugated to at least one of said scaffold protein, said membrane-forming lipid, or said antigen-binding polypeptide;

optionally wherein a spacer connects said functionalized group to said membrane-forming lipid and/or a spacer connects said complementary functional group to said antigen-binding polypeptide; and

wherein said conjugate translocates across the blood-brain barrier,

thereby delivering said biologically active agent or said detectable agent to ~~o~~the brain or central nervous system of an individual in need thereof.

~~178. The method of any one of claims 175-177, wherein said scaffold protein is apoE2 and/or apoE4.~~

~~179. The method of any one of claims 175-178, wherein said antigen-binding polypeptide is a Fab or a Fab-like molecule.~~

~~180. The method of any one of claims 175-179, wherein one or more of said membrane-forming lipids is a C_{4-28} fatty acyl and wherein said fatty acyl is conjugated to a short peptide of 20-60 amino acids.~~

~~181. The method of claim 180, wherein said fatty acyl is a C_{16} fatty acyl.~~

~~182. The method of claim 180 or 181, wherein said short peptide is a cystine knot peptide (CKP).~~

~~183. The method of claim 182, wherein the CKP is EETI-II-I, circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI-1, SOTI-1, circulin B, cyclopsychotride, or varv peptide A.~~

~~184. The method of claim 180 or 181, wherein the short peptide is CKP variant that comprises:~~

~~(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;~~

~~(b) one or more amino acid insertions, deletions, and/or substitutions at the N-terminus relative to a wild type CKP;~~

~~(c) one or more amino acid insertions, deletions, and/or substitutions at the C-terminus relative to a wild type CKP;~~

~~(d) a chemical modification at the N-terminus relative to a wild type CKP; and/or~~

~~(e) a chemical modification at the C-terminus relative to a wild type CKP.~~

185. The method of claim 184, wherein the CKP variant comprises an additional lysine residue at its N-terminus relative to a wild type CKP.

186. The method of claim 184 or 185, wherein the wild type CKP is EETI II.

187. The method of any one of claims 175-186, wherein said membrane forming lipids comprise a peptide-C_{4-28} fatty-acyl conjugate and at least one more of DMPC, DOPC, DOPS, DOPE, DPPC (*e.g.*, a peptide-C_{16} fatty acyl conjugate and DOPC) in the molar ratio of 1:3 to 1:15, or 1:6 to 1:12, or 1:9; and/or wherein said conjugate comprises 1-100, 10-90, 20-80, 30-70, 40-60, or 60 molecules of said short peptide.

188. The method of any one of claims 175-187, wherein said spacer is a PEG spacer that connects said functionalized group to said membrane-forming lipid.

189. The method of claim 188, wherein said PEG spacer has a MW of 1000-3000, 1500-2500, 1900-2200, or 2000.

190. The method of any one of claims 175-189, wherein said biologically active agent is a cytotoxic agent selected from the group consisting of daunomycin, doxorubicin, methotrexate, vindesine, a radionuclide, diphtheria toxin, ricin, geldanamycin, a maytansinoid, calicheamicin, and a combination of any one or more thereof.

191. The method of any one of claims 175-190, wherein said diagnostic agent is a label selected from the group consisting a radioactive isotope, a fluorophore, a chemiluminescent dye, a chromophore, an enzyme, a metal ion, a nanoparticle, and a combination of any one or more thereof.

192. The method of any one of claims 175-191, wherein the liquid formulation is administered intravenously.

193. The method of any one of claims 175-192, wherein said membrane forming lipids are conjugated to 5-100 molecules of said antigen binding polypeptide via a functionalized group on said membrane-forming lipid and a C-terminally located complementary functional group on said antigen binding polypeptide.

~~194. The method of any one of claims 175-193, wherein said antigen-binding polypeptide is a Fab and said Fab is connected via a PEG spacer to said membrane-forming lipid,~~

~~optionally wherein said PEG spacer connects said functionalized group to said membrane-forming lipid and has a MW of 1000-3000, 1500-2500, 1900-2200, or 2000.~~

~~195. The method of any one of claims 175-194, wherein said liquid formulation has a viscosity of 10-50 cP and a concentration of 100-300 mg of said conjugate/mL.~~

~~196~~24. A system or kit for delivering an antigen-binding polypeptide to a target cell, the system or kit comprising:

one or more components for preparing the conjugate of ~~any one of claims 1-7~~claim 1, ~~11-41,~~ or the ~~conjugate or~~ pharmaceutical composition of ~~any one of claims 42-46~~claim 3, or the formulation of claim ~~47~~4, wherein said components are provided in one or more compartments of said kit or system, and

optionally instructions for preparing said conjugate, composition, or formulation and/or instructions for delivering said antigen-binding polypeptide.

~~197~~25. A system or kit for delivering a short peptide of 20-60 amino acids (*e.g.* a cystine-knot peptide) to a target cell, the system or kit comprising:

one or more components for preparing the conjugate of ~~any one of claims 8-41~~claim 2, or the ~~conjugate or~~ pharmaceutical composition of ~~any one of claims 42-46~~claim 3, or the formulation of claim ~~47~~4, wherein said components are provided in one or more compartments of said kit or system, and

optionally instructions for preparing said conjugate or composition and/or instructions for delivering said short peptide (*e.g.*, said cystine-knot peptide).

~~198.~~26 A method of reducing lipid-scaffold protein conjugation in preparing a conjugate of a nanolipoprotein particle and an antigen-binding polypeptide, comprising:

a) providing a scaffold protein and a membrane-forming lipid under conditions allowing assembly of a nanolipoprotein particle comprising a lipid bilayer of said membrane-forming lipids encircled by said scaffold protein, wherein one or more of said membrane-forming lipids presents a functionalized group on one or both surfaces of said particle;

b) allowing said particle to contact an antigen-binding polypeptide (*e.g.*, a Fab) having a C-terminally located complementary functional group at a low pH that favors conjugation of said functionalized group to said functional group rather than to said scaffold protein; and

c) optionally purifying the conjugate of said particle and said antigen-binding polypeptide.

~~199. The method of claim 198, wherein said functionalized group does not conjugate to said scaffold protein at said low pH.~~

~~200. The method of claim 198 or 199, wherein said low pH is a pH of 5.5 to 6.5, a pH of 5-6, or a pH of 6.~~

~~201. The method of any one of claims 198-200, wherein said step b) follows said step a) without an intervening step to remove some or all unassembled membrane forming lipids.~~

~~202. The method of any one of claims 198-201, wherein said functionalized group is a maleimide derivative and wherein said functional group is a cysteine thiol group, optionally wherein said cysteine amino acid residue forms a hinge disulfide bond in the antibody from which the antigen binding polypeptide is derived (such as Cys-226 or Cys-227).~~

~~203. The method of any one of claims 198-202, wherein one or more of said membrane-forming lipids is a C_{4-28} fatty acyl and wherein said fatty acyl is conjugated to a short peptide of 20-60 amino acids.~~

~~204. The method of claim 203, wherein said fatty acyl is a C_{16} fatty acyl.~~

~~205. The method of claim 203 or 204, wherein said short peptide is a cystine knot peptide (CKP).~~

~~206. The method of claim 203, wherein the CKP is EETI-II I, circulin A, cyclopsychotride A, cycloviolacin O1, cycloviolacin O12, kalata B1, kalata B8, palicourein, tricyclon A, MCoTI 1, SOTI 1, circulin B, cyclopsychotride, or varv peptide A.~~

~~207. The method of claim 203 or 204, wherein the short peptide is CKP variant that comprises:~~

~~(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;~~

~~(b) one or more amino acid insertions, deletions, and/or substitutions at the N terminus relative to a wild type CKP;~~

~~(c) one or more amino acid insertions, deletions, and/or substitutions at the C terminus relative to a wild type CKP;~~

~~(d) a chemical modification at the N-terminus relative to a wild type CKP; and/or~~

~~(e) a chemical modification at the C terminus relative to a wild type CKP.~~

~~208. The method of any one of claims 203-207, wherein said membrane forming lipids comprise a peptide-C_{4-28} fatty acyl conjugate and at least one more of DMPC, DOPC, DOPS, DOPE, DPPC (*e.g.*, a peptide-C_{16} fatty acyl conjugate and DOPC) in the molar ratio of 1:3 to 1:15, or 1:6 to 1:12, or 1:9; and/or wherein said conjugate comprises 1-100, 10-90, 20-80, 30-70, 40-60, or 60 molecules of said short peptide.~~

~~209~~27. A method of increasing the biological activity of a short peptide attached to the surface of a lipid-based nanoparticle, comprising

(a) providing a lipid-based nanoparticle comprising a short peptide attached its surface, wherein one or more lipids of the lipid-based nanoparticle presents a functionalized group, and

(b) allowing the nanoparticle to contact a polypeptide having a functional group under conditions that favor conjugation of said functionalized group to said functional group.

~~210. The method of claim 209, further comprising purifying the conjugate comprising the lipid based nanoparticle, the short peptide, and the polypeptide.~~

~~211. The method of claim 209 or 210, wherein the lipid based nanoparticle comprises a lipid bilayer.~~

212. The method of claim 209 or 210, wherein the lipid-based nanoparticle is a liposome, a solid lipid nanoparticle (SLN), or a nanostructured lipid carrier (NLC).

213. The method of any one of claims 209-212, wherein a spacer connects said functionalized group to a lipid on the surface of the lipid-based nanoparticle and/or wherein a spacer connects said complementary functional group to said polypeptide.

214. The method of any one of claims 209-213, wherein the polypeptide is an antigen-binding polypeptide.

215. The method of claim 214, wherein the antigen-binding polypeptide is selected from the group consisting of a Fab, a Fab', a Fab'-SH, a $F(ab')_2$, a single chain Fab (scFab), a single chain Fv (scFv), a VH-VH dimer, a VL-VL dimer, a VH-VL dimer, a single domain, a diabody, a linear antibody, and a combination of any one or more thereof.

216. The method of any one of claims 209-215, wherein the short peptide is a CKP or a variant of a CKP that comprises:

(a) one or more amino acid insertions, deletions, and/or substitutions in one or more loop sequences relative to the corresponding one or more loop sequences of a wild type CKP;

(b) one or more amino acid insertions, deletions, and/or substitutions at the N terminus relative to a wild type CKP;

(c) one or more amino acid insertions, deletions, and/or substitutions at the C terminus relative to a wild type CKP;

(d) a chemical modification at the N terminus relative to a wild type CKP; and/or

(e) a chemical modification at the C terminus relative to a wild type CKP.

217. The method of any one of claims 209-216, wherein the activity of the short peptide following conjugation of the polypeptide is between 2-fold and 100-fold higher following conjugation of the polypeptide to the lipid-based nanoparticle as compared to the activity of the short peptide before conjugation of the polypeptide to the lipid-based nanoparticle.