

## CLAIMS

1. A composition for reducing adsorption of a therapeutic protein to one or more components of an intravenous drug delivery system, the composition comprising succinate and polysorbate 80.
2. The composition of claim 1, wherein the composition comprises:  
about 1 to about 10 mM succinate, and  
about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80.
3. The composition of claim 2, wherein the composition comprises about 4 mM to about 6 mM succinate.
4. The composition of claim 3, wherein the composition comprises about 5 mM succinate.
5. The composition of any one of claims 2-4, wherein the composition comprises about 0.002% (w/v) to about 0.008% (w/v) polysorbate 80.
6. The composition of claim 5, wherein the composition comprises about 0.004% (w/v) polysorbate 80.
7. The composition of any one of claims 2-6, wherein the pH of the composition is about 5.0 to about 7.0.
8. The composition of claim 7, wherein the pH of the composition is about 6.0.
9. The composition of any one of claims 1-8, wherein the composition comprises the therapeutic protein.
10. The composition of claim any one of claims 1-9, wherein the therapeutic protein comprises at least a first binding domain.
11. The composition of claim 10, wherein the first binding domain is a single chain variable fragment (scFv).

12. The composition of any one of claims 1-9, wherein the therapeutic protein comprises at least a first binding domain and a second binding domain.
13. The composition of claim 12, wherein the first binding domain is a single chain variable fragment (scFv) and the second binding domain is a scFv.
14. The composition of claim 12 or 13, wherein the first binding domain specifically binds to CD123.
15. The composition of any one of claims 12-14, wherein the second binding domain specifically binds CD3ε.
16. The composition of any one of claims 12-15, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:
- (a) the first binding domain
  - (b) a hinge region;
  - (c) an immunoglobulin constant region; and
  - (d) the second binding domain.
17. The composition of claim 16, wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.
18. The composition of any one of claims 12-17, wherein the first binding domain comprises:
- (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and
  - (ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.
19. The composition of claim 18, wherein the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HCDR3 comprises SEQ ID NO: 12.
20. The composition of claim 18, wherein the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15.

21. The composition of claim 18, wherein:  
the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11,  
and the HCDR3 comprises SEQ ID NO: 12; and  
the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14,  
and the LCDR3 comprises SEQ ID NO: 15.
22. The composition of any one of claims 12-21, wherein the first binding domain comprises a sequence at least 95% identical to SEQ ID NO: 18.
23. The composition of claim any one of claims 12-22, wherein the second binding domain comprises:  
(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and  
(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.
24. The composition of claim 23, wherein the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HCDR3 comprises SEQ ID NO: 21.
25. The composition of claim 23, wherein the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24.
26. The composition of claim 23, wherein:  
the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20,  
and the HCDR3 comprises SEQ ID NO: 21; and  
the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23,  
and the LCDR3 comprises SEQ ID NO: 24.
27. The composition of any one of claims 12-26, wherein the second binding domain comprises a sequence at least 95% or 100% identical to SEQ ID NO: 27.
28. The composition of any one of claims 12-27, wherein the therapeutic protein comprises the sequence of SEQ ID NO: 31.

29. The composition of claim 12 or 13, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain,

wherein the CD86 binding domain comprises a variable heavy chain and a variable light chain that specifically bind CD86,

wherein the immunoglobulin Fc domain is an IgG1 Fc domain that comprises two or more mutations that prevent or significantly reduce binding to Fc receptors FcγR, FcγRIIa, FcγRIIb, and FcγRIIIb,

wherein the monomeric IL-10 domain comprises two subunits of human IL-10 separated by a short linker, and

wherein the therapeutic protein is a homodimer.

30. The composition of claim 29, wherein the CD86 binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (2) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

31. The composition of claim 30, wherein the amino acid sequence of HCDR1 is SEQ ID NO: 1, the amino acid sequence of HCDR2 is SEQ ID NO: 2, the amino acid sequence of HCDR3 is SEQ ID NO: 3, the amino acid sequence of LCDR1 is SEQ ID NO: 4, the amino acid sequence of LCDR2 is SEQ ID NO: 5, and the amino acid sequence of LCDR3 is SEQ ID NO: 6.

32. The composition of any one of claims 29-31, wherein the CD86 binding domain comprises a variable heavy chain with an amino acid sequence at least 95% identical to SEQ ID NO: 7 and a variable light chain with an amino acid sequence at least 95% identical to SEQ ID NO: 8.

33. The composition of any one of claims 29-32, wherein the CD86 binding domain comprises an amino acid sequence that is at least about 95% or 100% identical to SEQ ID NO: 9.

34. The composition of any one of claims 29-33, wherein the monomeric IL-10 domain comprises an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 28.
35. The composition of any one of claims 29-34, wherein the therapeutic protein comprises SEQ ID NO: 30 or an amino acid sequence at least about 90%, at least about 95%, at least about 98%, or at least about 99% identical to SEQ ID NO: 30.
36. The composition of any one of claims 9-36, wherein the concentration of the therapeutic protein is about 0.01 µg/mL to about 2.0 µg/mL.
37. The composition of claim 36, wherein the concentration of the therapeutic protein is about 0.01, about 0.02, about 0.03, about 0.04, about 0.05, about 0.06, about 0.07, about 0.08, or about 0.09 µg/mL.
38. The composition of claim 36, wherein the concentration of the therapeutic protein is about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, or about 0.9 µg/mL.
39. The composition of claim 36, wherein the concentration of the therapeutic protein is about 1.0, about 1.1, about 1.2, about 1.3, about 1.4, about 1.5, about 1.6, about 1.7, about 1.8, about 1.9, or about 2.0 µg/mL.
40. The composition of any one of claim 1-39, wherein the composition comprises about 5 mM succinate and about 0.0004% (w/v) polysorbate 80 in water, wherein the pH of the composition is about 6.0, and wherein the composition is formulated for injection.
41. The composition of claim 1, wherein the composition comprises about 25 to about 150 mM succinate, and about 0.01% to about 0.1% (w/v) polysorbate 80.
42. The composition of claim 41, wherein the composition is at a 10X-50X concentration.
43. The composition of claim 42, wherein the composition is at a 20X concentration.

44. The composition of any one of claims 41-43, wherein the composition comprises about 75 mM to about 125 mM succinate.
45. The composition of claim 44, wherein the composition comprises about 100 mM succinate.
46. The composition of any one of claims 41-45, wherein the composition comprises about 0.05% (w/v) to about 0.1% (w/v) polysorbate 80.
47. The composition of claim 46, wherein the composition comprises about 0.08% (w/v) polysorbate 80.
48. The composition of any one of claims 41-47, wherein the pH of the composition is about 5.0 to about 7.0.
49. The composition of claim 48, wherein the pH of the composition is about 6.0.
50. The composition of any one of claims 41-49, wherein the composition comprises about 100 mM succinate and about 0.08% (w/v) polysorbate 80 in water, wherein the pH of the composition is about 6.0, and wherein the composition is formulated for injection.
51. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:  
about 100 mM succinate;  
about 0.08% (w/v) polysorbate 80; and  
about therapeutically effective amount of a therapeutic protein.
52. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:  
about 1 to about 10 mM succinate;  
about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and  
about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;  
wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:

- (a) a first binding domain that specifically binds to a first target;
  - (b) a hinge region;
  - (c) an immunoglobulin constant region; and
  - (d) a second binding domain that specifically binds to a second target.
53. The composition of claim 52, wherein the first target is CD86.
54. The composition of claim 52, wherein the first target is CD123.
55. The composition of claim 52, wherein the second target is a receptor of IL-10.
56. The composition of claim 52, wherein the second target is CD3ε.
57. The composition of claim 52, wherein the first target is CD86 and the second target is a receptor of IL-10.
58. The composition of claim 52, wherein the first target is CD123 and the second target is CD3ε.
59. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:  
about 1 to about 10 mM succinate,  
about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and  
about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;  
wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:  
(a) a first binding domain;  
(b) a hinge region;  
(c) an immunoglobulin constant region; and  
(d) a second binding domain;  
wherein the first binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3; wherein the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ

ID NO: 11, and the HDCR3 comprises SEQ ID NO: 12; and wherein the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15;

wherein the second binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3; wherein the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HDCR3 comprises SEQ ID NO: 21; and wherein the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24.

60. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;  
about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and  
about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;  
wherein the therapeutic protein comprises the sequence of SEQ ID NO: 31.

61. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;  
about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and  
about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;  
wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus: a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain,

wherein the CD86 binding domain comprises a variable heavy chain and a variable light chain that specifically bind CD86,

wherein the immunoglobulin Fc domain is an IgG1 Fc domain that comprises two or more mutations that prevent or significantly reduce binding to Fc receptors FcγR, FcγRIIa, FcγRIIb, and FcγRIIIb,

wherein the monomeric IL-10 domain comprises two subunits of human IL-10 separated by a short linker, and

wherein the therapeutic protein is a homodimer.

62. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;

wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus: a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain;

wherein the CD86 binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (2) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3, wherein the amino acid sequence of HCDR1 is SEQ ID NO: 1, the amino acid sequence of HCDR2 is SEQ ID NO: 2, the amino acid sequence of HCDR3 is SEQ ID NO: 3, the amino acid sequence of LCDR1 is SEQ ID NO: 4, the amino acid sequence of LCDR2 is SEQ ID NO: 5, and the amino acid sequence of LCDR3 is SEQ ID NO: 6;

wherein the monomeric IL-10 domain has an amino acid sequence of SEQ ID NO:28.

63. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;

wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus: a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain;

wherein the CD86 binding domain comprises the amino acid sequence of SEQ ID NO: 9; and

wherein the monomeric IL-10 domain comprises the amino acid sequence of SEQ ID NO: 28.

64. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;  
about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and  
about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;  
wherein the therapeutic protein comprises the amino acid sequence of SEQ ID  
NO: 30.

65. A container adapted for holding a therapeutic protein, wherein an interior surface of the container is first contacted with the composition of any one of claims 1-64 before it is contacted with a composition comprising the therapeutic protein.

66. The container of claim 65, wherein the container is substantially free of latex.

67. The container of any one of claims 65-66, wherein the container is substantially free of bis(2-ethylhexyl) phthalate (DEHP).

68. The container of any one of claims 65-67, wherein the container is selected from the group consisting of an IV bag, a syringe, and a tube.

69. A method of preparing an intravenous drug delivery system for delivery of a therapeutic protein, the method comprising:

providing at least one container adapted to hold the therapeutic protein; and  
before the therapeutic protein is added to the at least one container, contacting an interior surface of the at least one container with a composition comprising about 1 to about 10 mM succinate, and about 0.001% to 0.01% (w/v) polysorbate 80.

70. The method of claim 69, wherein the composition coats the interior surface of the at least one container and prevents the therapeutic protein from binding to the interior surface of the container.

71. The method of any one of claims 69-70, wherein the at least one container is substantially free of latex.

72. The method of any one of claims 69-71, wherein the at least one container is substantially free of bis(2-ethylhexyl) phthalate (DEHP).

73. The method of any one of claims 69-72, wherein the at least one container is selected from the group consisting of an IV bag, a syringe, and a tube.

74. A method of treating a subject by intravenous administration of a therapeutic protein, the method comprising:

providing at least one container adapted to hold the therapeutic protein;

contacting an interior surface of the container with a composition comprising about 1 to about 10 mM succinate and about 0.001% to about 0.01% (w/v) polysorbate 80;

contacting the interior surface of the container with a composition comprising the therapeutic protein; and

intravenously administering the therapeutic protein to the patient.

75. The method of claim 74, wherein the therapeutic protein comprises at least a first binding domain.

76. The method of claim 75, wherein the first binding domain is a single chain variable fragment (scFv).

77. The method of claim 74, wherein the therapeutic protein comprises at least a first binding domain and a second binding domain.

78. The method of claim 77, wherein the first binding domain is a single chain variable fragment (scFv) and the second binding domain is an scFv.

79. The method of any one of claims 77 or 78, wherein the first binding domain specifically binds to CD123.

80. The method of any one of claims 77 to 79, wherein the second binding domain specifically binds CD3ε.

81. The method of any one of claims 77 to 80, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:

(a) the first binding domain;

(b) a hinge region;

- (c) an immunoglobulin constant region; and
- (d) the second binding domain.

82. The method of claim 81, wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.

83. The method of any one of claims 77 to 82, wherein the first binding domain comprises:

- (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and
- (ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

84. The method of claim 83, wherein the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HCDR3 comprises SEQ ID NO: 12.

85. The method of claim 83, wherein the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15.

86. The method of claim 83, wherein:

the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HCDR3 comprises SEQ ID NO: 12; and

the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15.

87. The method of claim any one of claims 77 to 86, wherein the first binding domain comprises a sequence at least 95% or 100% identical to SEQ ID NO: 18.

88. The method of claim 77, wherein the second binding domain comprises:

- (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and
- (ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

89. The method of claim 88, wherein the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HCDR3 comprises SEQ ID NO: 21.
90. The method of claim 88, wherein the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24.
91. The method of claim 88, wherein:  
the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HCDR3 comprises SEQ ID NO: 21; and  
the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24.
92. The method of any one of claims 77-91, wherein the second binding domain comprises a sequence at least 95% identical to SEQ ID NO: 27.
93. The method of any one of claims 77-91, wherein the therapeutic protein comprises the sequence of SEQ ID NO: 31.
94. The method of any one of claims 77-80, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain;  
wherein the CD86 binding domain comprises a variable heavy chain and a variable light chain that specifically bind CD86;  
wherein the immunoglobulin Fc domain is an IgG1 Fc domain that comprises two or more mutations that prevent or significantly reduce binding to Fc receptors FcγR, FcγRIIa, FcγRIIb, and FcγRIIIb;  
wherein the monomeric IL-10 domain comprises two subunits of human IL-10 separated by a short linker; and  
wherein the therapeutic protein is a homodimer.
95. The method of claim 94, wherein the CD86 binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and

HCDR3; and (2) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

96. The method of claim 95, wherein the amino acid sequence of HCDR1 is SEQ ID NO 1, the amino acid sequence of HCDR2 is SEQ ID NO: 2, the amino acid sequence of HCDR3 is SEQ ID NO: 3, the amino acid sequence of LCDR1 is SEQ ID NO: 4, the amino acid sequence of LCDR2 is SEQ ID NO: 5, and the amino acid sequence of LCDR3 is SEQ ID NO: 6.

97. The method of any one of claims 94-96, wherein the CD86 binding domain comprises a variable heavy chain with an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 7 and a variable light chain with an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 8.

98. The method of any one of claims 94-97, wherein the CD86 binding domain comprises an amino acid sequence with at least about 95% or 100% identical to SEQ ID NO: 9.

99. The method of any one of claims 94-98, wherein the monomeric IL-10 domain comprises an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 28.

100. The method of any one of claims 94-99, wherein the therapeutic protein comprises SEQ ID NO: 30 or an amino acid sequence at least about 90%, at least about 95%, at least about 98%, or at least about 99% identical to SEQ ID NO: 30.

101. The method of any one of claims 74-100 wherein the therapeutic protein is administered by intravenous infusion.

102. The method of any one of claims 74-101, wherein the composition coats an interior surface of the at least one container and prevents the therapeutic protein from binding to the interior surface of the container.

103. The method of any one of claims 74-102, wherein the subject is a mammal.

104. The method of claim 103, wherein the subject is a human.

105. A drug delivery system for delivering a therapeutic protein to a patient, the system comprising:

at least one container adapted to hold the therapeutic protein;

wherein an interior surface of the at least one container is contacted with a composition comprising about 1 to about 10 mM succinate, and about 0.001% to 0.01% (w/v) polysorbate 80 before it is contacted with a composition comprising the therapeutic protein.