

CLAIMS:

1. A polyacrylamide-based copolymer comprising:
a water-soluble carrier monomer selected from the group consisting of *N*-(3-methoxypropoyl)acrylamide (MPAM), 4-acryloylmorpholine (MORPH), *N,N*-
5 dimethylacrylamide (DMA), *N*-hydroxyethyl acrylamide (HEAM), and acrylamide (AM); and
a functional dopant monomer selected from the group consisting of *N*-[tris(hydroxymethyl)-methyl]acrylamide (TRI), 2-acrylamido-2-methylpropane sulfonic acid (AMP), (3-acrylamidopropyl)trimethylammonium chloride (TMA), *N*-
10 isopropylacrylamide (NIP), *N-tert*-butylacrylamide (TBA), and *N*-phenylacrylamide (PHE).
2. The copolymer of claim 1, wherein:
the water-soluble carrier monomer is selected from the group consisting of *N*-(3-methoxypropoyl)acrylamide (MPAM) and 4-acryloylmorpholine (MORPH); and
15 the functional dopant monomer is selected from the group consisting of *N*-isopropylacrylamide (NIP) and *N*-phenylacrylamide (PHE).
3. The copolymer of claim 1 or 2, wherein the weight percent (wt%) of the water-soluble carrier monomer is about 70% to about 98%, about 75% to about 95%, or about 80% to about 95%.
- 20 4. The copolymer of any one of claims 1-3, wherein the weight percent (wt%) of the functional dopant monomer is about 2% to about 30%, about 5% to about 25%, or about 5% to about 20%.
5. The copolymer of claim 1 or 2, wherein the functional dopant monomer is NIP and is about 5% to about 30%, about 10% to about 28%, about 2% to about 30%,
25 about 5% to about 26%, or about 20% to about 26% by weight of the copolymer.
6. The copolymer of claim 5, wherein the water-soluble carrier monomer is MORPH.
7. The copolymer of claim 5, wherein the water-soluble carrier monomer is MPAM.

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8. The copolymer of claim 1, wherein the functional dopant monomer is selected from the group consisting of AMP, TMA, TBA, and PHE and is about 2% to about 16%, about 12% to about 15%, about 5% to about 15%, or about 6% to about 14% by weight of the copolymer.
- 5 9. The copolymer of claim 8, wherein the water-soluble carrier monomer is MORPH.
10. The copolymer of claim 8, wherein the water-soluble carrier monomer is MPAM
- 10 11. The copolymer of any one of claims 8-10, wherein the functional dopant monomer is PHE.
12. The copolymer of claim 1, wherein the functional dopant monomer is TRI and is about 3% to about 17%, about 4% to about 6%, about 7% to about 12%, or about 13% to about 17% by weight of the copolymer.
- 15 13. The copolymer of any one of claims 1-12, wherein the degree of polymerization is about 10 to about 500, about 20 to about 200, or about 50.
14. The copolymer of any one of claims 1-13, wherein the molecular weight of the copolymer is about 1,000 to about 40,000 g/mol, about 1,000 to about 30,000 g/mol, about 2,000 to about 10,000 g/mol, about 3,000 to about 7,000 g/mol, or about 4,000 to about 6,000 g/mol.
- 20 15. The copolymer of any one of claims 1-14, wherein the functional dopant monomer is hydrophobic.
16. The copolymer of any one of claims 1-15, wherein the copolymer is amphiphilic.
- 25 17. A polyacrylamide-based copolymer comprising:
a water-soluble carrier monomer comprising an acrylamide reactive moiety; and
a functional dopant monomer comprising an acrylamide reactive moiety;
wherein:

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the weight percent (wt%) of the water-soluble carrier monomer is about 70% to about 98%;

the weight percent (wt%) of the functional dopant monomer is about 2% to about 30%;

5 the average molecular weight (M_n) of the polyacrylamide-based copolymer is about 1,000 g/mol to about 30,000 g/mol; and

the degree of polymerization is about 10 to about 250.

18. The copolymer of claim 17, wherein the water-soluble carrier monomer is selected from the group consisting of *N*-(3-methoxypropoyl)acrylamide (MPAM), 4-
10 acryloylmorpholine (MORPH), *N,N*-dimethylacrylamide (DMA), *N*-hydroxyethyl acrylamide (HEAM), and acrylamide (AM).

19. The copolymer of claim 18, wherein the water-soluble carrier monomer is selected from the group consisting of *N*-(3-methoxypropoyl)acrylamide (MPAM) and 4-acryloylmorpholine (MORPH).

15 20. The copolymer of any one of claims 17-19, wherein the functional dopant monomer is selected from the group consisting of *N*-[tris(hydroxymethyl)-methyl]acrylamide (TRI), 2-acrylamido-2-methylpropane sulfonic acid (AMP), (3-acrylamidopropyl)trimethylammonium chloride (TMA), *N*-isopropylacrylamide (NIP), *N*-*tert*-butylacrylamide (TBA), and *N*-phenylacrylamide (PHE).

20 21. The copolymer of claim 20, wherein the functional dopant monomer is selected from the group consisting of *N*-isopropylacrylamide (NIP) and *N*-phenylacrylamide (PHE).

22. A composition comprising the polyacrylamide-based copolymer of any one of claims 1-21 and a pharmaceutically acceptable excipient.

25 23. A composition comprising the copolymer of any one of claims 1-21, wherein the composition is a cosmetic product, a hair product, a lotion, a food product, a veterinary product, or a nutritional product.

24. A composition comprising the copolymer of any one of claims 1-21 and a protein.

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25. The composition of claim 24, wherein the protein is a protein susceptible to aggregation in an aqueous medium.

26. The composition of claim 24 or 25, wherein the protein is selected from the group consisting of antibodies and fragments thereof, cytokines, chemokines,
5 hormones, vaccine antigens, cancer antigens, adjuvants, and combinations thereof.

27. The composition of any one of claims 24-26, wherein the composition comprises the protein in a concentration at least two times greater, at least three times greater, at least four times greater, or at least five times greater than the concentration of the same protein in the composition without the copolymer.

10 28. The composition of claim 26 or 27, wherein the protein is a monoclonal antibody.

29. The composition of any one of claims 24-28, wherein the protein is insulin, or an analog thereof.

30. The composition of claim 29, wherein the insulin, or an analog thereof, is
15 selected from the group consisting of porcine insulin, bovine insulin, feline insulin, human insulin, recombinant insulin, insulin lispro, HUMALOG[®], insulin glargine, LANTUS[®], insulin detemir, LEVEMIR[®], ACTRAPID[®], modern insulin, NOVORAPID[®], VELOSULIN[®], HUMULIN[®] M3, HYPURIN[®], INSUMAN[®], INSULATARD[®], MIXTARD[®] 30, MIXTARD[®] 40, MIXTARD[®] 50, insulin aspart,
20 insulin glulisine, insulin isophane, insulin degludec, insulin icodec, insulin zinc extended, NOVOLIN[®] R, HUMULIN[®] R, HUMULIN[®] R regular U-500, NOVOLIN[®] N, HUMULIN[®] N, RELION[®], AFREZZA[®], HUMULIN[®] 70/30, NOVOLIN[®] 70/30, NOVOLOG[®] 70/30, HUMULIN[®] 50/50, HUMALOG[®] mix 75/25, insulin aspart protamine-insulin aspart, insulin lispro protamine-insulin lispro, insulin lispro protamine-insulin lispro,
25 insulin lispro, human insulin NPH-human insulin regular, insulin degludec-insulin aspart, and combinations thereof.

31. The composition of claim 30, wherein the insulin, or an analog thereof, is a human insulin or a recombinant human insulin.

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32. The composition of any one of claims 29-31, wherein the insulin, or an analog thereof, comprises about 50% or greater, about 60% or greater, about 70% or greater, about 80% or greater, about 90% or greater, or about 99% or greater insulin present in monomeric form.

5 33. The composition of any one of claims 29-32, wherein the insulin concentration is about 0.34 mg/mL (10 U/mL) to about 34 mg/mL (1000 U/mL), about 1.7 mg/mL (50 U/mL) to about 17 mg/mL (500 U/mL), about 3.4 mg/mL (100 U/mL), about 6.8 mg/mL (200 U/mL), or about 10.2 mg/mL (300 U/mL).

10 34. The composition of any one of claims 24-33, wherein the copolymer concentration is about 0.0001% to about 5%, about 0.001% to about 1% by weight, about 0.005% to about 0.5% by weight, about 0.005% to about 0.02% by weight, about 0.01% to about 0.2% by weight, about 0.1% to about 0.4% by weight, or about 0.2% to about 0.3% by weight, about 0.005% by weight, about 0.01% by weight, about 0.05% by weight, about 0.1% by weight, or about 1% by weight of the composition.

15 35. The composition of any one of claims 24-34, wherein the composition comprises one or more of an aqueous buffer, tonicity modifier, and preservative, and combinations thereof.

36. The composition of any one of claims 24-35, wherein the pH of the composition is about 4 to about 9 or about 7.4.

20 37. The composition of any one of claims 29-36, further comprising glucagon, a GLP-1 agonist, a glucose-dependent insulinotropic polypeptide (GIP), or a dual GIP and GLP-1 agonist.

38. The composition of claim 37, wherein the GLP-1 agonist is selected from the group consisting of lixisenatide, liraglutide, albiglutide, dulaglutide, exenatide, 25 extended-release exenatide, and semaglutide.

39. The composition of claim 37, wherein the dual GIP and GLP-1 agonist is tirzepatide.

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40. The composition of any one of claims 29-36, further comprising amylin, or an analog thereof.

41. The composition of claim 40, wherein the amylin analog is pramlintide.

42. The composition of claim 40 or 41, wherein the amylin, or an analog thereof, and insulin, or an analog thereof are present in a ratio of about 1:1 to about 1:20, about 1:1 to about 1:15, about 1:1 to about 1:10, about 1:1 to about 1:6, or about 1:20, about 1:15, about 1:10, about 1:9, about 1:8, about 1:7, about 1:6, about 1:5, about 1:4, about 1:3, about 1:2, or about 1:1.

43. The composition of any one of claims 24-42, suitable for human or veterinary administration.

44. A composition comprising:
about 0.01 wt% of a polyacrylamide-based copolymer comprising:
about 74% to about 80% by weight of a MORPH carrier monomer; and
about 20% to about 26% by weight of a NIP dopant monomer; and
about 100 U/mL insulin, or an analog thereof.

45. A composition comprising:
about 0.01 wt% of a polyacrylamide-based copolymer comprising:
about 74% to about 80% by weight of a MORPH carrier monomer; and
about 20% to about 26% by weight of a NIP dopant monomer;
about 100 U/mL insulin, or an analog thereof; and
about 0.5 mg/mL to about 0.6 mg/mL pramlintide.

46. The composition of claim 45, wherein the pH of the composition is about 6 to about 8.

47. The composition of claim 45 or 46, wherein the insulin, or analog thereof, is substantially present in monomeric form.

48. The composition of any one of claims 29-47, wherein the copolymer stabilizes the insulin such that the insulin exhibits increased stability when stored at room

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temperature as compared to the same insulin composition that does not contain the copolymer.

49. The composition of claim 48, wherein the increased stability is at least 10-fold, at least 15-fold, at least 20-fold, at least 25-fold, at least 30-fold, at least 35-fold, at least 40-fold, at least 45-fold, at least 50-fold, or greater as compared to the same insulin composition that does not contain the copolymer.

50. The composition of any one of claims 29-49, wherein the insulin, or an analog thereof, comprises about 60% or greater, about 70% or greater, about 80% or greater, about 90% or greater, or about 99% or greater insulin in monomeric form.

51. The composition of any one of claims 22-50, wherein the composition is aqueous.

52. A method of treating an elevated glucose level in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition of any one of claims 29-51, wherein the elevated glucose level is associated with insulin deficiency in the subject.

53. A method of managing the blood glucose level in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition of any one of claims 29-51.

54. A method for increasing thermal stability of a protein formulation, comprising adding about 0.0005 wt% to about 5 wt% of the copolymer of any one of claims 1-21 to the protein formulation.

55. A method for increasing stability of a protein formulation, comprising adding about 0.005 wt% to about 5 wt% of the copolymer of any one of claims 1-21 to the protein formulation.

56. A method for reducing the rate of aggregation of a protein in an aqueous composition, comprising adding about 0.005 wt% to about 5 wt% of the copolymer of any one of claims 1-21 to the protein formulation.

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57. The method of any one of claims 54-56, wherein the protein is a protein that tends to aggregate in an aqueous medium.

58. The method of any one of claims 54-57, wherein the protein is selected from the group consisting of antibodies and fragments thereof, cytokines, chemokines,
5 hormones, vaccine antigens, cancer antigens, adjuvants and combinations thereof.

59. The method of any one of claims 54-58, wherein the protein is a monoclonal antibody.

60. The method of any one of claims 54-58, wherein the protein is a vaccine antigen.

10 61. The method of any one of claims 54-58, wherein the protein is insulin, or an analog thereof.

62. The method of claim 61, wherein the insulin, or an analog thereof, is selected from the group consisting of porcine insulin, bovine insulin, feline insulin, human insulin, recombinant insulin, insulin lispro, HUMALOG[®], insulin glargine,
15 LANTUS[®], insulin detemir, LEVEMIR[®], ACTRAPID[®], modern insulin, NOVORAPID[®], VELOSULIN[®], HUMULIN[®] M3, HYPURIN[®], INSUMAN[®], INSULATARD[®], MIXTARD[®] 30, MIXTARD[®] 40, MIXTARD[®] 50, insulin aspart, insulin glulisine, insulin isophane, insulin degludec, insulin icodec, insulin zinc extended, NOVOLIN[®] R, HUMULIN[®] R, HUMULIN[®] R regular U-500, NOVOLIN[®]
20 N, HUMULIN[®] N, RELION[®], AFREZZA[®], HUMULIN[®] 70/30, NOVOLIN[®] 70/30, NOVOLOG[®] 70/30, HUMULIN[®] 50/50, HUMALOG[®] mix 75/25, insulin aspart protamine-insulin aspart, insulin lispro protamine-insulin lispro, insulin lispro protamine-insulin lispro, human insulin NPH-human insulin regular, insulin degludec-insulin aspart, and combinations thereof.

25 63. The method of claim 62, wherein the insulin, or an analog thereof, is a human insulin or a recombinant human insulin.

64. The method of any one of claims 61-63, wherein the insulin is human insulin.

65. The method of claim 64, wherein the copolymer increases the time to aggregation of the human insulin formulation by at least 10-fold, at least 15-fold, at least 20-fold, at least 25-fold, at least 30-fold, at least 35-fold, at least 40-fold, at least 45-fold, or at least 50-fold when stored at 37 °C as assessed by a transmittance assay as compared
5 to a human insulin formulation that does not contain the copolymer.

66. The method of claim 64 or 65, wherein the copolymer increases the time to aggregation of the human insulin formulation by at least 10-fold, at least 15-fold, at least 20-fold, at least 25-fold, at least 30-fold, at least 35-fold, at least 40-fold, at least 45-fold, or at least 50-fold when stored at 50 °C as assessed by a transmittance assay as
10 compared to a human insulin formulation that does not contain the copolymer.

67. The method of any one of claims 64 to 66, wherein addition of the copolymer maintains the *in vitro* bioactivity of the human insulin formulation for at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, or at least 6 months.

15 68. The method of any one of claims 52-67, wherein the composition is aqueous.

69. The method of any one of claims 52-68, wherein the composition is administered via infusion pumps or artificial pancreas closed-loop systems.