CLAIMS

1. A method of producing a composition comprising a substantially homogenous population of XTEN sequences, the method comprising:

a. providing a polypeptide composition comprising at least one polypeptide having an amino acid sequence selected from the group of sequences set forth in Table 6, wherein the amino acid sequence comprises at least one cleavage sequence,

b. treating said polypeptide composition with trypsin under conditions effective to cleave the cleavage sequence; and

wherein at least 95%, 96%, 97%, 98%, or 99% of individual sequences in the resulting substantially homogeneous population of XTEN sequences have an identical sequence length.

2. The method of claim 1, further comprising:

a. adsorbing the XTEN sequences onto a chromatography substrate under conditions effective to capture the XTEN sequences but not the protease;

b. eluting the XTEN sequences; and

c. recovering the XTEN sequences wherein at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of individual molecules of the population have an identical sequence length.

3. The method of claim 2, wherein the chromatography substrate is an anion exchange substrate.

4. The method of claim 3, wherein the anion exchange substrate is selected from the group consisting of macrocap Q, capto Q, superQ-650M, and poros D.

5. The method of any one of claims 1-4, wherein the XTEN sequence has at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to a sequence selected from the group of amino acid sequences set forth in Table 6.

6. The method of any one of claims 1-5, wherein the XTEN sequence has at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to a sequence selected from the group of amino acid sequences set forth in Tables 2 or 3.

7. A composition produced by the method of any one of claims 1-6.

8. A composition comprising a substantially homogenous population of polypeptides comprising an extended recombinant polypeptide (XTEN), and wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of individual polypeptide molecules in said population have an identical sequence length.

9. The composition of claim 8, wherein the XTEN is characterized in that:

a. the XTEN comprises about 36 to about 3000 amino acid residues;

b. the sum of glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P) residues constitutes more than about 90% of the total amino acid residues of the XTEN;

c. the XTEN sequence is substantially non-repetitive such that (i) the XTEN sequence contains no three contiguous amino acids that are identical unless the amino acids are serine, (ii) at least about 80% of the XTEN sequence consists of non-overlapping sequence motifs, each of the sequence motifs comprising about 9 to about 14 amino acid residues, wherein any two contiguous amino acid residues does not occur more than twice in each of the sequence motifs; or (iii) the XTEN sequence has a subsequence score of less than 10;

d. the XTEN sequence has greater than 90% random coil formation as determined by GOR algorithm;

e. the XTEN sequence has less than 2% alpha helices and 2% beta-sheets as determined by Chou-Fasman algorithm; and

f. the XTEN sequence lacks a predicted T-cell epitope when analyzed by TEPITOPE algorithm, wherein the TEPITOPE algorithm prediction for epitopes within the XTEN sequence is based on a score of –9.

10. The composition of claim 8, wherein the XTEN comprises a sequence having at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of the sequences set forth in Table 2, Table 3, Table 4 and Tables 22-25.

11. The composition of claim 8, further comprising a first affinity tag.

12. The composition of claim 11, wherein the first affinity tag has binding affinity for a chromatography substrate selected from the group consisting of hydrophobic interaction chromatography (HIC) substrate, cation exchange substrate, anion exchange substrate, immobilized metal ion affinity chromatography (IMAC) substrate, and immobilized antibody substrate.

13. The composition of claim 11, wherein the first affinity tag is selected from the group consisting of the sequences set forth in Table 7.

14. The composition of any one of claims 11-13, further comprising a helper sequence.

15. The composition of claim 14, wherein the helper sequence comprises a sequence having at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of the sequences set forth in Table 10.

16. The composition of claim 14, wherein the helper sequence is selected from the group consisting of

a. KNPEQAEEQX1EET wherein X1 is independently S or R;

b. ANPEQAEEQX1EET wherein X1 is independently S or R;

c. KNPEQAEEQAEEQX1EET wherein X1 is independently S or R;

d. KX2X3EQAEEQAEEQX1EET wherein X1 is independently S or R, X2 is independently K or N, and X3 is independently K, N, T, Q, H, P, E, D, A, R, or S;

e. KX2(X3)10QX1EET wherein X1 is independently S or R, X2 is independently K or N, and X3 is independently K, N, T, Q, H, P, E, D, A, R, or S;

f. KX2(X3)7AEEQX1EET wherein X1 is independently S or R, X2 is independently K or N, and X3 is independently K, N, T, Q, H, P, E, D, A, R, or S;

g. KX2X3EQE(X3)3AEEQREET wherein X2 is independently K or N, and X3 is independently K, N, T, Q, H, P, E, D, A, R, or S;

h. KX2X3EQE(X3)3AEE(X3)5 wherein X2 is independently K or N, and X3 is independently K, N, T, Q, H, P, E, D, A, R, or S;

i. KKQEQEKEQAEEQ(X4X5)2REET wherein X4 is independently A or S and X5 is independently K, Q, or E; KKQEQEKEQAEEQ(X4X5)4REET wherein X4 is independently A or S and X5 is independently K, Q, or E;

j. KKQEQEKEQAEEQ(Z)4REET, wherein Z is any naturally-occurring L-amino acid;

k. KX2(X3)n, wherein n is an integer from 10-40 and X2 is independently K or N, and X3 is independently K, N, T, Q, H, P, E, D, A, R, or S;

l. (X3)n wherein n is an integer from10-50 and X3 is independently K, N, T, Q, H, P, E, D, A, R, or S;

m. KX2QEQEKEQAEEQ(X4X5)nX1EET wherein n is zero or an integer from 1-10 and X1 is independently S or R, X2 is independently K or N, X4 is independently A or S, and X5 is independently K, Q, or E;

n. KX2(X3)n(X4X5)mX1EET, wherein n is an integer from 5-20, m is zero or an integer from 1-10, X1 is independently S or R, X2 is independently K or N, X3 is independently K, N, T, Q, H, P, E, D, A, R, or S, X4 is independently A or S, and X5 is independently K, Q, or E; and

o. KX2(X3)n(Z)mX1EET, wherein n is an integer from 5-20, m is zero or an integer from 1-10, X1 is independently S or R, X2 is independently K or N, X3 is independently K, N, T, Q, H, P, E, D, A, R, or S, and Z is any naturally-occurring L-amino acid.

17. The composition of any one of claims 11-16, further comprising a first cleavage sequence, wherein the first cleavage sequence is selected from the group consisting of the sequences set forth in Table 8 and Table 9.

18. The composition of claim 17, wherein the composition has the configuration of formula I:

(HS)-(AT1)-(CS1)-(XTEN) I

wherein

a. HS is the helper sequence;

b. AT1 is the first affinity tag;

c. CS1 is the first cleavage sequence; and

d. XTEN is the extended recombinant polypeptide.

19. The composition of claim 17, further comprising a second cleavage sequence wherein the first and the second cleavage sequences are capable of being cleaved by the same protease, and wherein the composition has the configuration of formula II:

(HS)-(CS1)-(XTEN)-(CS2)-(AT1) II

wherein

a. HS is a helper sequence;

b. AT1 is the first affinity tag;

c. CS1 is the first cleavage sequence;

d. CS2 is the second cleavage sequence; and

e. XTEN is the extended recombinant polypeptide.

20. The composition of claim 18 or claim 19, wherein the first affinity tag comprises the sequence RPRPRPRPRPRPR or HHHHHH.

21. The composition of any one of claims 11-17, further comprising a second affinity tag and a second cleavage sequence, wherein the second affinity tag has binding affinity to a different chromatography substrate than the first affinity tag, wherein the chromatography substrate is selected from the group consisting of a HIC substrate, cation exchange substrate, anion exchange substrate, IMAC substrate, and immobilized antibody substrate, and wherein the first and the second cleavage sequences are capable of being cleaved by the same protease.

22. The composition of claim 21, wherein the second affinity tag is different from the first affinity tag and is the second affinity tag is selected from the group of sequences set forth in Table 7.

23. The composition of claim 21 or claim 22, wherein the composition has the configuration of formula III:

(HS)-(AT1)-(CS1)-(XTEN)-(CS2)-(AT2) III

wherein

a. HS is the helper sequence;

b. AT1 is the first affinity tag;

c. CS1 is the first cleavage sequence;

d. CS2 is the second cleavage sequence;

e. XTEN is the extended recombinant polypeptide; and

f. AT2 is the second affinity tag.

24. The composition of claim 23, wherein the first affinity tag comprises the sequence RPRPRPRPRPRPR and the second affinity tag comprises the sequence HHHHHH.

25. The composition of claim 23, wherein the first affinity tag comprises the sequence HHHHHH and the second affinity tag comprises the sequence RPRPRPRPRPRPR.

26. A composition comprising a substantially homogenous population of a polypeptide obtained by the process comprising:

a. culturing a host cell that comprises a vector encoding the polypeptide in a fermentation reaction under conditions effective to express the polypeptide as a component of a crude expression product of the host cell, wherein the encoded polypeptide comprises an XTEN, a first cleavage sequence and a first affinity tag;

b. adsorbing the polypeptide of the crude expression product onto a first chromatography substrate under conditions effective to capture the first affinity tag onto the first chromatography substrate;

c. eluting the polypeptide; and

d. recovering the polypeptide wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of the polypeptides of the population have an identical sequence length.

27. The composition of claim 26, wherein the first chromatography substrate is selected from the group consisting of a HIC substrate, cation exchange substrate, anion exchange substrate, and IMAC substrate.

28. The composition of claim 26, wherein the affinity tag is selected from the group consisting of the affinity tags of Table 7.

29. The composition of claim 27, wherein the first chromatography substrate is cation exchange and the first affinity tag comprises the sequence RPRPRPRPRPRPR.

30. The composition of claim 27, wherein the first chromatography substrate is IMAC and the first affinity tag comprises the sequence HHHHHHHHH.

31. The composition of claim 26, wherein the vector encodes the polypeptide of any one of claims 11-19.

32. The composition of any one of claims 26-28, wherein the vector further encodes a second cleavage sequence and a second affinity tag wherein the first and the second cleavage sequences are capable of being cleaved by the same protease and wherein the second affinity tag has binding affinity to a second, different chromatography substrate than the first affinity tag, and wherein the composition is obtained by the process further comprising:

a. adsorbing the polypeptide onto a second chromatography substrate under conditions effective to capture the second affinity tag onto the second chromatography substrate;

b. eluting the polypeptide; and

c. recovering the polypeptide wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of the polypeptides of the population have an identical sequence length.

33. The composition of claim 32, wherein the vector encodes the polypeptide of claim 23.

34. The composition of claim 32, wherein first chromatography substrate is different from the second chromatography substrate and each of the first and the second chromatography substrate are independently selected from the group consisting of HIC, cation exchange, anion exchange, and IMAC.

35. The composition of claim 32, wherein the first chromatography substrate is cation exchange and the first affinity tag comprises the sequence RPRPRPRPRPRPR and the second chromatography substrate is IMAC and the first affinity tag comprises the sequence HHHHHHHH.

36. The composition of claim 32, wherein the first chromatography substrate is IMAC and the first affinity tag comprises the sequence HHHHHHHH and the second chromatography substrate is cation exchange and the first affinity tag comprises the sequence RPRPRPRPRPRPR.

37. The composition of any one of claims 23-28 or 32-34, the process further comprising:

a. treating the composition with a protease under conditions effective to cleave the cleavage sequence(s), thereby releasing the XTEN from the affinity tag(s);

b. adsorbing the XTEN onto a chromatography substrate under conditions effective to capture the XTEN but not the affinity tag(s) or the protease;

c. eluting the XTEN; and

d. recovering the XTEN wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of the individual molecules of XTEN have an identical sequence length.

38. The composition of claim 37, wherein the cleavage sequence(s) are capable of being cleaved by a protease selected from the group consisting of the proteases of Table 9.

39. The composition of claim 38, wherein the cleavage sequence(s) are capable of being cleaved by trypsin wherein the sequence is selected from the group consisting of the sequences set forth in Table 8, and wherein the protease is trypsin.

40. The composition of claims 37 or 38, wherein the chromatography substrate is anion exchange.

41. The composition of claim 40, wherein the anion exchange chromatography substrate is selected from the group consisting of macrocap Q, capto Q, superQ-650M, and poros D.

42. The composition of any one of claims 23-28 or 32-34, the process further comprising:

a. treating the composition with a protease under conditions effective to cleave the cleavage sequence(s), thereby releasing the XTEN from the affinity tag(s);

b. adsorbing the protease onto a chromatography substrate under conditions effective to capture the protease but not the XTEN; and

c. recovering the XTEN from the eluate wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of the individual molecules of XTEN have an identical sequence length.

43. The composition of claim 42, wherein the cleavage sequence(s) are capable of being cleaved by a protease selected from the group consisting of the proteases of Table 9.

44. The composition of claim 42 or claim 43, wherein the cleavage sequence(s) are capable of being cleaved by trypsin wherein the sequence is selected from the group consisting of the sequences set forth in Table 8, and wherein the protease is trypsin.

45. The composition of any one of claims 42-44, wherein the chromatography substrate is one or more of cation exchange substrate, HIC substrate or IMAC substrate.

46. A composition comprising an XTEN sequence, wherein the XTEN sequence further comprises one or more cleavage sequences capable of being cleaved by trypsin and wherein treatment with trypsin under conditions effective to cleave all the cleavage sequences results in a preparation of XTEN fragments wherein each XTEN fragment has at least about 95%, 96%, 97%, 98%, or 99% sequence identity to every other fragment in the preparation.

47. The composition of claim 46, wherein the cleavage sequence has at least 86% sequence identity to or is identical to the sequence SASRSA or SASKSA.

48. The composition of claim 46, wherein the cleavage sequence comprises the sequence RX or KX, wherein X is any L-amino acid other than proline.

49. The composition of claim 46, wherein the composition has at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to the sequences selected from the group of sequences set forth in Table 6.

50. A method for producing an XTEN sequence in a host cell, the method comprising culturing a host cell that comprises a vector encoding a polypeptide comprising a) the XTEN sequence and b) a helper sequence, in a fermentation reaction under conditions effective to express the polypeptide as a component of a crude expression product at a concentration of more than about 2 grams/liter (g/L), or about 3 g/L, or about 4 g/L, or about 5 g/L, or about 6 g/L, or about 7 g/L of said polypeptide.

51. A method for producing an XTEN sequence in a host cell, the method comprising culturing a host cell that comprises a vector encoding a polypeptide comprising a) the XTEN sequence and b) a helper sequence, in a fermentation reaction under conditions effective to express the polypeptide as a component of a crude expression product at a concentration of more than about 10 milligrams/gram of dry weight host cell (mg/g), or at least about 15 mg/g, or at least about 20 mg/g, or at least about 25 mg/g, or at least about 30 mg/g, or at least about 40 mg/g, or at least about 50 mg/g of said polypeptide.

52. A method for producing an XTEN sequence in a host cell, the method comprising culturing a host cell that comprises a vector encoding a polypeptide comprising a) the XTEN sequence and b) a helper sequence, in a fermentation reaction under conditions effective to express the polypeptide as a component of a crude expression product at a concentration of more than about 10 milligrams/gram of dry weight host cell (mg/g), or at least about 250 micromoles/L, or about 300 micromoles/L, or about 350 micromoles/L, or about 400 micromoles/L, or about 450 micromoles/L, or about 500 micromoles/L of said polypeptide.

53. The method of any one of claims 50-52, wherein the concentration is measured when the fermentation reaction reaches an optical density of at least 130 at a wavelength of 600 nm.

54. The method of any one of claims 50-52, wherein the helper sequence of the expressed polypeptide is at the N-terminus of the polypeptide and wherein the helper sequence has at least about 90%, 91%, 92%, 93%, 94%, or 95% sequence identity or is identical to a sequence selected from the group consisting of the sequences set forth in Table 10.

55. The method of claim 54, wherein the vector encodes the polypeptide of any one of claims 14-17.

56. The method of claim 55, further comprising

a. recovering the crude expression product of the host cell fermentation reaction mixture;

b. adsorbing the polypeptide of the crude expression product onto a first chromatography substrate under conditions effective to capture the first affinity tag of the polypeptide onto the chromatography substrate, wherein the first chromatography substrate is selected from the group consisting of a HIC substrate, a cation exchange substrate, an anion exchange substrate, and an IMAC substrate;

c. eluting and recovering the XTEN sequence wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of the polypeptides have an identical sequence length.

57. The method of any one of claims 50-52, wherein the vector encodes the polypeptide of any one of claims 21-23.

58. The method of claim 57, further comprising:

a. recovering the crude expression product of the host cell fermentation reaction mixture;

b. adsorbing the polypeptide onto a first chromatography substrate under conditions effective to capture the first affinity tag of the polypeptide onto the chromatography substrate wherein the first chromatography substrate is selected from the group consisting of a HIC substrate, a cation exchange substrate, an anion exchange substrate, and an IMAC substrate;

c. eluting the polypeptide;

d. adsorbing the polypeptide onto a second chromatography substrate under conditions effective to capture the second affinity tag of the polypeptide onto the chromatography substrate

wherein the second chromatography substrate is selected from the group consisting of a HIC substrate, a cation exchange substrate, an anion exchange substrate, and an IMAC substrate;

e. eluting the polypeptide; and

f. recovering the XTEN sequence wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of the polypeptides have an identical sequence length.

59. The method of claim 56 or claim 58, the method further comprising:

a. treating the polypeptide with a protease under conditions effective to cleave the cleavage sequence, thereby releasing the XTEN from the polypeptide;

b. adsorbing the XTEN onto an anion chromatography substrate under conditions effective to capture the XTEN;

c. eluting the XTEN; and

d. recovering the XTEN wherein at least 90%, or at least 91%, or at least 92%, or at least 93%, or at least 94%, or at least 95% of the individual XTEN molecules have an identical sequence length.

60. The method of claim 59, wherein the anion chromatography substrate is selected from the group consisting of macrocap Q, capto Q, superQ-650M, and poros D.

61. The method of claim 59 or claim 60, wherein the protease is trypsin and wherein the sequence is selected from the group consisting of the sequences set forth in Table 8.

62. The method of claim 56 or claim 58, the method further comprising:

a. treating the polypeptide with a protease under conditions effective to cleave the cleavage sequence(s), thereby releasing the XTEN from the polypeptide;

b. adsorbing the protease onto a chromatography substrate under conditions effective to capture the protease but not the XTEN; and

c. recovering the XTEN in the eluate wherein at least 90%, 91%, 92%, 93%, 94%, or 95% of the XTEN have an identical sequence length.

63. The method of claim 62, wherein the protease is trypsin, and wherein the sequence is selected from the group consisting of the sequences set forth in Table 8.

64. The method of claim 62 or claim 63, wherein the chromatography substrate is one or more of a HIC substrate, a cation exchange substrate, and an IMAC substrate.

65. A solid support comprising immobilized thereon a population of substantially identical polypeptides, wherein the solid support comprises a chromatography substrate, and the immobilized polypeptides each comprise an XTEN, a first affinity tag, and a second affinity tag, wherein:

a. the first affinity tag is joined to the XTEN by a cleavage sequence at the N-terminus of the XTEN;

b. the second affinity tag is joined to the XTEN by a cleavage sequence at the C-terminus of the XTEN;

c. the second affinity tag is different from the first affinity tag;

d. the chromatography substrate is capable of binding to either said first or said second affinity tag but not both; and

e. at least 90%, 91%, 92%, 93%, 94%, or 95% of the immobilized polypeptide molecules have an identical sequence length.

66. The solid support of claim 65, wherein the immobilized polypeptide molecules comprise the polypeptides any one of claims 21-25.

67. The solid support of claim 65 or claim 66, wherein the cleavage sequence has at least about 86% sequence identity to or is identical to the sequence SASRSA or SASKSA.

68. The solid support of claim 65 or claim 66, wherein the cleavage sequence comprises the sequence RX or KX, wherein X is any L-amino acid other than proline.

69. The solid support of any one of claims 65-68, wherein the solid support is selected from the group consisting of HIC chromatography resin, cation exchange chromatography resin, anion exchange chromatography resin, and IMAC chromatography resin.

70. The composition of claim 69, wherein the first affinity tag comprises the sequence RPRPRPRPRPRPR and the second affinity tag comprises the sequence HHHHHH.

71. The composition of claim 69, wherein the first affinity tag comprises the sequence HHHHHH and the second affinity tag comprises the sequence RPRPRPRPRPRPR.

72. A conjugate composition comprising an XTEN covalently linked to one or more molecules of at least a first cross-linker, wherein the cross-linker is selected from the group consisting of the cross-linkers set forth in Table 13, the alkyne reactants set forth in Table 15, and the azide reactants set forth in Table 15, and the XTEN is selected from the group consisting of the XTEN of claim 37, the XTEN of claim 42, the XTEN of claim 7, the sequences set forth in Table 2, and the sequences set forth in Table 3.

73. The conjugate composition of claim 72, wherein the first cross-linker is conjugated to the at least first XTEN at a location selected from the group consisting of:

a. an alpha-amino group of an N-terminal amino acid residue of the XTEN;

b. an epsilon amino group of each lysine residue of the XTEN; and

c. a thiol group of each cysteine residue of the XTEN.

74. The conjugate composition of claim 72 or claim 73, wherein the XTEN has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group of sequences set forth in Table 2 and Table 3.

75. The conjugate composition of claim 74, wherein the XTEN is selected from the group consisting of AE144, AE288, AE432, AE576, AE864, Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199, and the cross-linker is conjugated to the alpha amino-group of the N-terminal amino acid of the XTEN.

76. The conjugate composition of claim 74, wherein the XTEN is selected from the group consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3, and the cross-linker is conjugated to the thiol group of each cysteine residue of the XTEN.

77. The conjugate of any one of claims 72-76, wherein the first cross-linker is selected from the group consisting of an N-maleimide, an iodoacetyl reagent, a pyridyl disulfide reagent, a vinyl sulfone reagent, 3-propargyloxypropanoic acid, (oxyethyl)n-acetylene where n is 1-10, dibenzylcyclooctyne (DBCO), cyclooctyne (COT), 3-azide-propionic acid, 6-azide-hexanoic acid, and (oxyethyl)n-azide where n is 1-10.

78. The conjugate composition of claim 76, wherein the first cross-linker is conjugated to the thiol group of each cysteine residue of the XTEN, and the conjugate further comprises a second cross-linker conjugated to the alpha amino-group of the N-terminal amino acid of the XTEN wherein the cross-linker is selected from the group consisting of the cross-linkers set forth in Table 13, the alkyne reactants of Table 15, and the azide reactants of Table 15.

79. The conjugate composition of claim 78, having the configuration of formula V:
wherein independently for each occurrence;

a. CL1 is the first cross-linker conjugated to cysteine residues of the XTEN;

b. CL2 is the second cross-linker conjugated to XTEN at the N-terminus;

c. x is an integer of 1 to about 10;

d. y is an integer of 1 with the proviso that x + y is > 2;

e. XTEN is a cysteine engineered XTEN comprising x number of cysteine residues.

80. The conjugate composition of any one of claims 72-77, further comprising a single atom residue of a first payload conjugated to each first cross-linker wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur.

81. The conjugate composition of claim 80, wherein the first payload of the single atom residue is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21.

82. The conjugate composition of any one of claims 72-77, further comprising a payload selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21 conjugated to each first cross-linker.

83. The conjugate composition of claim 78 or claim 79, further comprising a single atom residue of a first payload conjugated to each of the first cross-linkers wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur, and a single atom residue of a second payload conjugated to the second cross-linker wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur.

84. The conjugate composition of claim 83, wherein the first payload of the single atom residue is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21 and the second payload of the single atom residue is a different payload from the first payload and is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21.

85. The conjugate composition of claim 78 or claim 79, further comprising a first payload conjugated to each of the first cross-linkers wherein the payload is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21, and a second payload different from the first payload conjugated to the second cross-linker wherein the second payload is selected from the group consisting of payloads set forth in Tables 6, 7, 18, and 21.

86. The conjugate composition of claim 78 or claim 79, further comprising a first payload conjugated to each of the first cross-linkers wherein the payload is selected from the group consisting drug moieties of Table 21, and a second payload different from the first payload conjugated to the second cross-linker wherein the second payload is selected from the group consisting of targeting moieties of Table 21.

87. The conjugate composition of claim 85 or claim 86, wherein the second payload is linked to the N-terminus of the XTEN by the second cross-linker conjugated by reaction of an alkyne reactant and an azide reactant selected from the group consisting of the reactants of Table 15.

88. A conjugate composition comprising at least a first and a second XTEN, wherein the XTEN are the same or are different and each is selected from the group consisting of the XTEN of claim 37, the XTEN of claim 42, the XTEN of claim 7, and the sequences set forth in Table 3, and in which the first and the second XTEN are conjugated to each other by the N-termini of the first and the second XTEN with a cross-linker created by reaction of an alkyne reactant and an azide reactant selected from the group consisting of the reactants of Table 15.

89. The conjugate composition of claim 88, wherein the first XTEN and the second XTEN are different and each independently has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group of sequences set forth in Table 3.

90. The conjugate composition of claim 89, wherein the first XTEN has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at

least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group of sequences consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3 and the second XTEN has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a different sequence selected from the group of sequences consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3.

91. The conjugate composition of claim 88, wherein the first XTEN and the second XTEN are the same are each has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group of sequences set forth in Table 3.

92. The conjugate composition of claim 91, wherein the first XTEN and the second XTEN each have at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group of sequences consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3.

93. The conjugate composition of any one of claims 88-92, wherein the first and the second XTEN each comprises one or more cysteine residues, and further comprises a first cross-linker conjugated to each cysteine residue of the first XTEN and a second cross-linker conjugated to each cysteine residue of the second XTEN, wherein the first and the second cross-linkers are independently selected from the group consisting of the cross-linkers set forth in Table 13.

94. The conjugate composition of any one of claims 88-92, wherein the first and the second XTEN each comprises one or more lysine residues, and further comprises a cross-linker conjugated to each lysine residue of the first and/or the second XTEN of the conjugate, wherein the cross-linker is selected from the group consisting of the cross-linkers set forth in Table 13.

95. The conjugate composition of claim 93 or claim 94, further comprising a single atom residue of a first payload conjugated to each cross-linker of the first XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur, and further comprises a single atom residue of a second payload conjugated to each cross-linker of the second XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur.

96. The conjugate composition of claim 95, wherein the first payload of the single atom residue is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21, and the second payload of the single atom residue is a different payload from the first payload and is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21.

97. The conjugate composition of claim 93 or claim 94, further comprising a first payload conjugated to each cross-linker of the first XTEN wherein the first payload is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21, and further comprises a second payload different from the first payload wherein the second payload is conjugated to each cross-linker of the second XEN wherein the second payload is selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21.

98. The conjugate composition of claim 93 or claim 94, further comprising a first payload conjugated to each cross-linker of the first XTEN wherein the first payload is selected from the group consisting of the targeting moieties set forth in Table 18, and further comprises a second payload different from the first payload wherein the second payload is conjugated to each cross-linker of the second XTEN wherein the second payload is selected from the group of toxins set forth in Table 18.

99. The conjugate composition of claim 93 or claim 94, further comprising a first payload conjugated to each cross-linker of the first XTEN wherein the first payload is selected from the group consisting of the targeting moieties set forth in Table 21, and further comprises a second payload different from the first payload wherein the second payload is conjugated to each cross-linker of the second XTEN wherein the second payload is selected from the group of toxins set forth in Table 21.

100. The conjugate composition of claim 99, wherein the first XTEN is Seg 176 of Table 3 and the second XTEN is selected from the group consisting of Seg 176 and Seg 177 set forth in Table 3.

101. A conjugate composition comprising at least a first XTEN, a second XTEN, and a third XTEN wherein the XTEN are each independently selected from the group consisting of the XTEN of claim 37, the XTEN of claim 42, the XTEN of claim 7, and the sequences set forth in Table 3, wherein the the first and the second and the third XTEN are conjugated to each other at the N-termini using a trivalent cross-linker selected from the group consisting of the trivalent cross-linkers set for in Table 13 or Table 14.

102. The conjugate composition of claim 100, wherein the trivalent cross-linker is selected from the group consisting of Tris-(2-Maleimidoethyl)amine (TMEA) and amine-reactive Tris-(succinimidyl aminotricetate) (TSAT).

103. The conjugate composition of any one of claims 100-102, wherein the first, the second, and the third XTEN are the same and each has at least about 90%, or at least about 91%, or at

least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3.

104. The conjugate composition of any one of claims 100-102, wherein the first and the second XTEN are the same and each has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3, and the third XTEN is different from the first and the second XTEN and has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3.

105. The conjugate composition of claim 103 or claim 104, wherein the conjugate further comprises a first cross-linker conjugated to each cysteine residue of the first XTEN, a second cross-linker conjugated to each cysteine residue of the second XTEN, and a third cross-linker conjugated to each cysteine residue of the third XTEN, wherein the cross-linker is selected from the group consisting of the cross-linkers set forth in Table 13.

106. The conjugate composition of claim 105, having the configuration of formula XII:

(CL1)x-(XTEN1)-3xCL-(XTEN2)-(CL2)y

|

(XTEN3)-(CL3)z XII

wherein independently for each occurrence;

a. 3xCL is the trivalent cross-linker;

b. CL1 is the first cross-linker conjugated to XTEN1;

c. CL2 is the second cross-linker conjugated to XTEN2;

d. CL3 is the third cross-linker conjugated to XTEN3;

e. x is an integer of 1 to about 10;

f. y is an integer of 1 to about 10;

g. z is an integer of 1 to about 10 with the proviso that x + y + z is > 3;

h. XTEN1 is the first XTEN;

i. XTEN2 is the second XTEN; and

j. XTEN3 is the third XTEN.

107. The conjugate composition of claim 105 or claim 106, further comprising

a. a single atom residue of a first payload conjugated to each first cross-linker of the first XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur;

b. a single atom residue of a second payload conjugated to each second cross-linker of the second XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur; and

c. a single atom residue of a third payload conjugated to each third cross-linker of the third XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur.

108. The conjugate composition of claim 105 or claim 106, further comprising

a. a first payload conjugated to each first cross-linker of the first XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18 and 21;

b. a second payload conjugated to each second cross-linker of the second XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18 and 21, wherein the payload is the same or is different from the first payload; and

c. a third payload conjugated to each third cross-linker of the third XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18 and 21, wherein the third payload is the same or is different from the first or the second payload.

109. The conjugate composition of claim 108, wherein the first payload is a targeting moiety with specific binding affinity to a target, wherein the targeting moiety is selected from the group consisting of the targeting moieties set forth in Tables 17-19 and 21, and the second and the third payloads are a drug, which may be the same or may be different and wherein the drug is selected from the group consisting of the drugs set forth in Table 6, Table 18, and Table 21.

110. The conjugate composition of claim 109, wherein the targeting moiety is selected from the group consisting of LHRH and folate, and wherein the drug is selected from the group consisting of doxorubicin, paclitaxel, auristatin, monomethyl auristatin E (MMAE), monomethyl auristatin F, maytansine, dolastatin, calicheamicin, vinca alkaloid, camptothecin, mitomycin C, epothilone, hTNF, Il-12, bortezomib, ranpirnase, pseudomonas exotoxin, SN-38, and rachelmycin.

111. The conjugate composition of claim 108, wherein the targeting moiety, and the drug moiety correspond to any one of conjugates 1-290 set forth in Table 21.

112. The conjugate composition of claim 111, wherein the conjugate has the XTEN, the targeting moiety, and the drug moiety corresponding to conjugate 71 of Table 21.

113. A conjugate composition comprising at least a first and a second and a third and a fourth XTEN, wherein the XTEN are selected from the group consisting of the XTEN of claim 37, the XTEN of claim 42, the XTEN of claim 7, and the sequences set forth in Table 3, wherein the XTEN may be the same or different, and in which the first and the second and the third and the fourth XTEN are conjugated to each other by the N-terminus using a tetravalent cross-linker wherein the tetravalent cross-linker is a tetravalent maleimide cluster.

114. The conjugate composition of claim 113, wherein the first, the second, the third, and the fourth XTEN are the same and each has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3.

115. The conjugate composition of claim 113, wherein the first and the second XTEN are the same and each has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3, and the third and the fourth XTEN are the same but are different from the first and the second XTEN and each has at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group consisting of Seg 174, Seg 175, Seg 176, Seg 177, Seg 186, Seg 187, Seg 188, Seg 189, Seg 190, Seg 191, Seg 192, Seg 193, Seg 194, Seg 195, Seg 196, Seg 197, Seg 198, and Seg 199 set forth in Table 3.

116. The conjugate composition of claim 114 or claim 115, wherein the conjugate further comprises a first cross-linker conjugated to each cysteine residue of the first XTEN, a second cross-linker conjugated to each cysteine residue of the second XTEN, a third cross-linker conjugated to each cysteine residue of the third XTEN, and a fourth cross-linker conjugated to each cysteine residue of the fourth XTEN, wherein each cross-linker is selected from the group consisting of the cross-linkers set forth in Table 13.

117. The conjugate composition of any one of claim 116, having the configuration of formula XIV

(CL1)v-(XTEN1)-4xCL-(XTEN2)-(CL2)x

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(CL3)y-(XTEN3) (XTEN4)-(CL4)z XIV

wherein independently for each occurrence:

a. 4xCL is the tretravalent cross-linker;

b. CL1 is the first cross-linker conjugated to XTEN1;

c. CL2 is the second cross-linker conjugated to XTEN2;

d. CL3 is the third cross-linker conjugated to XTEN3;

e. CL4 is the fourth cross-linker conjugated to XTEN4;

f. v is an integer of 1 to about 10;

g. x is an integer of 1 to about 10;

h. y is an integer of 1 to about 10;

i. z is an integer of 1 to about 10 with the proviso that x + y + z is > 4;

j. XTEN1 is the first XTEN;

k. XTEN2 is the second XTEN;

l. XTEN3 is the third XTEN; and

m. XTEN4 is the fourth XTEN.

118. The conjugate composition of claim 116 or claim 117, further comprising

a. a single atom residue of a first payload conjugated to each first cross-linker of the first XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur;

b. a single atom residue of a second payload conjugated to each second cross-linker of the second XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur;

c. a single atom residue of a third payload conjugated to each third cross-linker of the third XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur; and

d. a single atom residue of a fourth payload conjugated to each fourth cross-linker of the fourth XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur..

119. The conjugate composition of claim 116 or claim 117, further comprising

a. a first payload conjugated to each first cross-linker of the first XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21;

b. a second payload conjugated to each second cross-linker of the second XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21, wherein the payload is the same or is different from the first payload;

c. a third payload conjugated to each third cross-linker of the third XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21, wherein the payload is the same or is different from the first or the second payload; and

d. a fourth payload conjugated to each fourth cross-linker of the fourth XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18, and 21, wherein the payload is the same or is different from the first or the second or the third payload.

120. The conjugate composition of claim 119, wherein the first payload is a targeting moiety with specific binding affinity to a target wherein the targeting moiety is selected from the group consisting of the targeting moieties set forth in Tables 17-19 and 21, and at least one other of the second, third, and fourth payloads is a drug wherein the drug is selected from the group consisting of the drugs set forth in Tables 6, 18 and 21.

121. The conjugate composition of claim 120, wherein the targeting moiety is selected from the group consisting of LHRH and folate, and the drug is selected from the group consisting of doxorubicin, paclitaxel, auristatin, maytansine, dolastatin, calicheamicin, vinca alkaloid, camptothecin, mitomycin C, epothilone, hTNF, Il-12, bortezomib, ranpirnase, pseudomonas exotoxin, SN-38, and rachelmycin.

122. The conjugate composition of claim 119, wherein the first payload is a targeting moiety with specific binding affinity to a target wherein the targeting moiety is selected from the group consisting of the targeting moieties set forth in Tables 17-19 and 21, and at least one other of the second, third, and fourth payloads is a drug wherein the drug is selected from the group consisting of the drugs set forth in Tables 6, 18 and 21, and wherein the XTEN, the targeting moiety, and the drug moiety correspond to any one of conjugates 1-290 set forth in Table 21.

123. The conjugate composition of claim 101, having the configuration of formula XVI:

$$(CL1)x\text{-}(XTEN1)\text{-}3xCL\text{-}(XTEN2)\text{-}(CL2)y$$
$$|$$
$$(XTEN3) \qquad \text{XVI}$$

wherein independently for each occurrence;

a. 3xCL is the trivalent cross-linker;

b. CL1 is the first cross-linker conjugated to XTEN1;

c. CL2 is the second cross-linker conjugated to XTEN2;

d. x is an integer of 1 to about 10;

e. y is an integer of 1 to about 10 with the proviso that x + y is > 2;

f. XTEN1 is the first XTEN;

g. XTEN2 is the second XTEN; and

h. XTEN3 is the third XTEN wherein the XTEN is selected from the group consisting of the sequences set forth in Table 2.

124. The conjugate composition of claim 123, further comprising

a. a single atom residue of a first payload conjugated to each first cross-linker of the first XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur; and

b. a single atom residue of a second payload conjugated to each second cross-linker of the second XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur.

125. The conjugate composition of claim 123, further comprising:

a. a first payload conjugated to each first cross-linker of the first XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18 and 21; and

b. a second payload conjugated to each second cross-linker of the second XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18 and 21, wherein the payload is the same or is different from the first payload.

126. The conjugate composition of claim 125, wherein the first payload is a targeting moiety with specific binding affinity to a target, wherein the targeting moiety is selected from the group consisting of the targeting moieties set forth in Tables 17-19 and 21, and the second payload is a drug, which may be the same or may be different and wherein the drug is selected from the group consisting of the drugs set forth in Table 6, Table 18, and Table 21.

127. The conjugate composition of claim 126, wherein the targeting moiety is selected from the group consisting of LHRH and folate, and wherein the drug is selected from the group consisting of doxorubicin, paclitaxel, auristatin, monomethyl auristatin E (MMAE), monomethyl auristatin F, maytansine, dolastatin, calicheamicin, vinca alkaloid, camptothecin, mitomycin C, epothilone, hTNF, Il-12, bortezomib, ranpirnase, pseudomonas exotoxin, SN-38, and rachelmycin.

128. The conjugate composition of claim 125, wherein the first payload is selected from the group consisting of the drugs of Table 11 and the proteins of Table 12 and the second payload is different from the first payload and is selected from the group consisting of the drugs of Table 11 and the proteins of Table 12.

129. The conjugate composition of claim 125, wherein the first payload and the second payload are identical and are selected from the group consisting of the drugs of Table 11 and the proteins of Table 12.

130. The conjugate composition of claim 101, having the configuration of formula XVII:

(CL1)x-(XTEN1)-3xCL-(XTEN2)

|

(XTEN3) XVII

wherein independently for each occurrence;

a. 3xCL is the trivalent cross-linker;

b. CL1 is the first cross-linker conjugated to XTEN1;

c. x is an integer of 1 to about 10;

d. XTEN1 is the first XTEN wherein the XTEN is selected from the group consisting of the sequences set forth in Table 3;

e. XTEN2 is the second XTEN wherein the XTEN is selected from the group consisting of the sequences set forth in Table 2; and

f. XTEN3 is the third XTEN wherein the XTEN is selected from the group consisting of the sequences set forth in Table 2.

131. The conjugate composition of claim 130, further comprising a single atom residue of a first payload conjugated to each first cross-linker of the first XTEN wherein the residue is selected from the group consisting of carbon, nitrogen, oxygen and sulfur.

132. The conjugate composition of claim 130, further comprising a first payload conjugated to each first cross-linker of the first XTEN selected from the group consisting of the payloads set forth in Tables 6, 7, 18 and 21.

133. A composition comprising multimeric branched XTEN molecules, wherein a solution of the composition has a viscosity that is less than a solution comprising a corresponding linear XTEN having the same number of amino acids and the same molar concentration.

134. The composition of claim 133, wherein the XTEN molecules have a trimeric, tetrameric, or pentameric configuration.

135. The composition of claim 133, wherein the XTEN molecules are selected from the group consisting of the sequences set forth in Table 2 and Table 3.

136. The composition of any one of claims 133-135, wherein the viscosity of the solution is reduced by at least 5, 6, 7, 8, 9 or 10 cP in a solution containing ≧100 mg/ml of the multimeric XTEN compared to a solution containing ≧100 mg/ml of the corresponding linear XTEN of equal molar concentration.

137. A polypeptide having at least about 90%, or at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99%, or 100% sequence identity to a sequence selected from the group of sequences set forth in Table 52.

138. A pharmaceutical composition, comprising the conjugate of any one of claims 85-87, 97-99, 108-112, 118-122, 125-127, 129 or 132 and a pharmaceutically acceptable carrier.

139. The pharmaceutical composition of claim 138 for treatment of a condition selected from the group of conditions set forth in Table 16.

140. The pharmaceutical composition of claim 138 for use in a pharmaceutical regimen for treatment of a subject, said regimen comprising the pharmaceutical composition.

141. The pharmaceutical composition of claim 140, wherein the pharmaceutical regimen further comprises the step of determining the amount of pharmaceutical composition needed to achieve a beneficial effect in a subject having a condition selected from the group of conditions set forth in Table 16.

142. The pharmaceutical composition of claim 141, wherein the pharmaceutical regimen for treating the subject comprises administering the pharmaceutical composition in two or more successive doses to the subject at an effective amount, wherein the administration results in at least a 10%, or 20%, or 30%, or 40%, or 50%, or 60%, or 70%, or 80%, or 90% greater improvement of at least one, two, or three parameters associated with the condition compared to an untreated subject.

143. A conjugate of any one of claims 85-87, 97-99, 108-112, 118-122, 125-127, 129 or 132 for use in the preparation of a medicament for treatment of a condition selected from the group of conditions set forth in Table 16.

144. A method of selecting a combination of payloads linked to XTEN as a therapeutic agent, the method comprising

a. providing a library of XTENs comprising a plurality of XTEN sequences wherein each of said XTEN sequences is conjugated to at least a first payload and at least a second payload which is different from the first payload;

b. from said library, selecting an XTEN sequence as the therapeutic agent if it exhibits an improved in vitro or in vivo parameter as compared to that of (1) an XTEN sequence conjugated to the first payload alone; and (2) an XTEN sequence conjugated to the second payload alone.

145. The method of claim 144, wherein first payload and second payload are therapeutically effective for ameliorating a common disease.

146. The method of claim 144, wherein the first drug and second drug are therapeutically effective for treating different symptoms of a common disease.

147. The method of claim 145 or claim 146, wherein the common disease is selected from cancer, cancer supportive care, cardiovascular, central nervous system, endocrine disease, gastrointestinal, genitourinary, hematological, HIV infection, hormonal disease, inflammation, autoimmune disease, infectious disease, metabolic disease, musculoskeletal disease, nephrology disorders, ophthalmologic diseases, pain, and respiratory.

148. The method of claim 144, wherein the first payload and second payload mediate their therapeutic effect via a common biological pathway.

149. The method of claim 144, wherein the first payload and second payload are different drugs selected from the group consisting of the drugs set forth in Table 6, Table 18 and Table 21.

150. The method of claim 144, wherein the first payload and second payload are different biologically active proteins selected from the group consisting of the proteins set forth in Table 7, Table 18 and Table 21.

151. The method of claim 144, wherein the first payload is a drug selected from the group consisting of the drugs set forth in Table 6, Table 18 and Table 21 and the second payload is a biologically active protein selected from the group consisting of the proteins set forth in Table 7, Table 18 and Table 21.

152. An isolated polypeptide comprising an extended recombinant polypeptide (XTEN) that is linked to an affinity purification tag via a proteolytic cleavage site having a sequence selected from SASRSA or SASXSA where X is R or K.

153. A polypeptide comprising an extended recombinant polypeptide (XTEN) that is linked at its N-terminus to a first affinity purification tag via a proteolytic cleavage site having a sequence selected from SASRSA or SASXSA where X is R or K, and at its C-terminus to a second affinity purification tag via a proteolytic cleavage site having a sequence selected from SASRSA or SASXSA where X is R or K.

154. A composition having the structure set forth in FIG. 117.