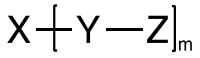
We claim:

1. A composition comprising a compound of Formula 1:



Formula 1

where:

m is an integer from 1 to 100;

X comprises an antigen which induces an unwanted immune response, or a tolerogenic portion thereof;

wherein X comprises:

a self-antigen;

a transplant antigen,

a food, fungus, dust, cat, mouse, dog, horse or plant antigen, or

a therapeutic agent that is not naturally occurring;

Y comprises a linker moiety; and

Z comprises a liver-targeting moeity;

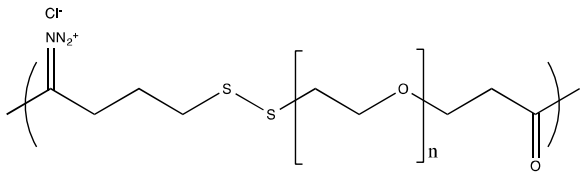
wherein Z comprises galactose, galactosamine, and/or N-acetylgalactosamine.

2. The composition of claim 1 where Z is conjugated to Y at the C1, C2 or C6 of Z.

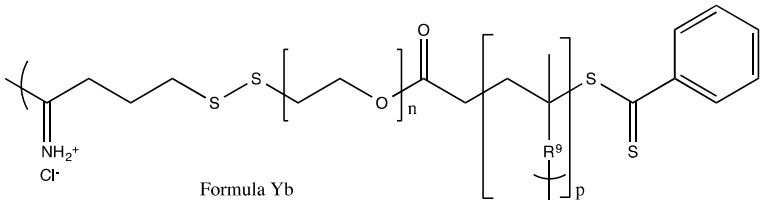
3. The composition of claim 1 where Y is prepared using one or more N-hydroxysuccinamidyl linkers, malaemide linkers, vinylsulfone linkers, pyridyl di-thiol-poly(ethylene glycol) linkers, pyridyl di-thiol linkers, n-nitrophenyl carbonate linkers, NHS-ester linkers, and nitrophenoxy poly(ethylene glycol)ester linkers.

4. The composition of claim 1 where Y comprises one or more of:

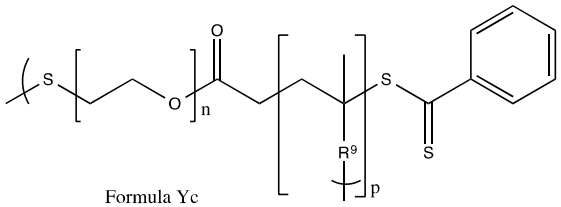
a disulfanyl ethyl ester, a sulfide of a disulfide bond, and/or a structure represented by one of Formulae Ya to Yp:



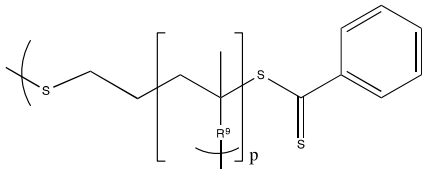
Formula Ya



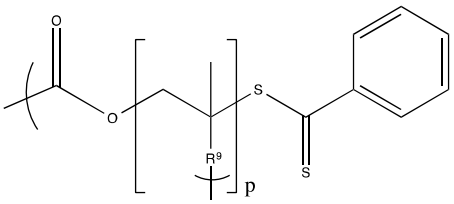
Formula Yb



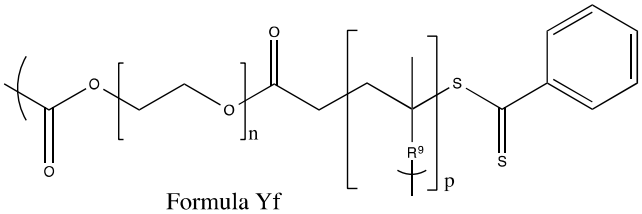
Formula Yc



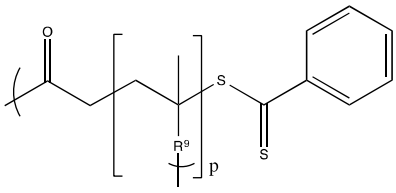
Formula Yd



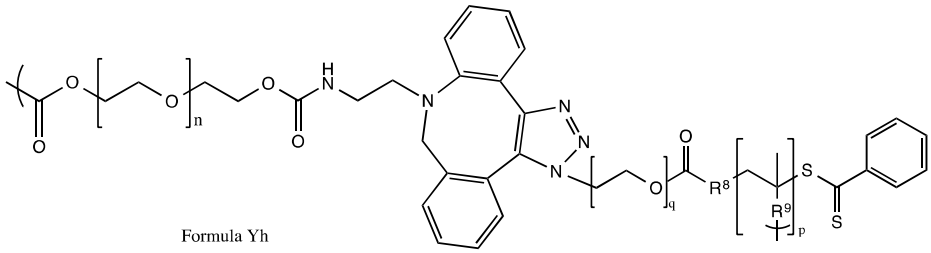
FormulaYe



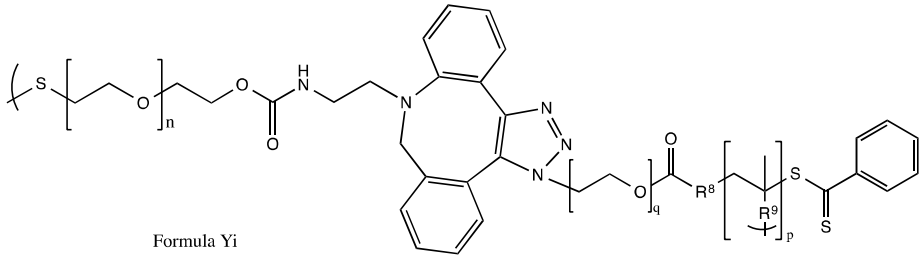
Formula Yf



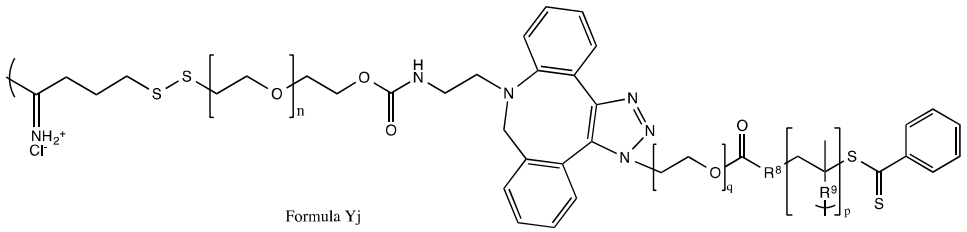
Formula Yg



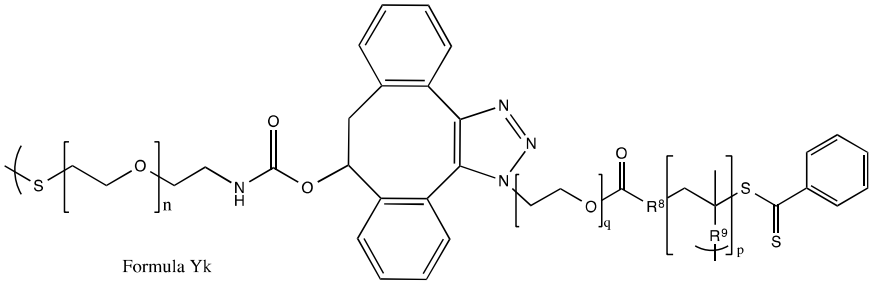
Formula Yh



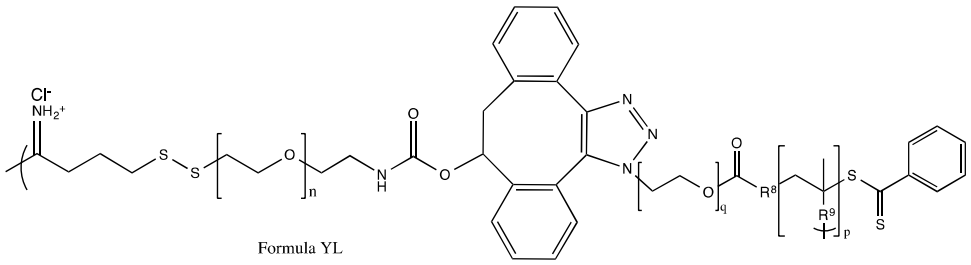
Formula Yi



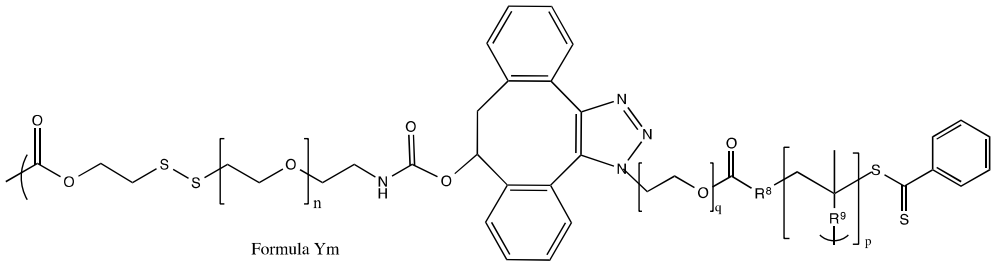
Formula Yj



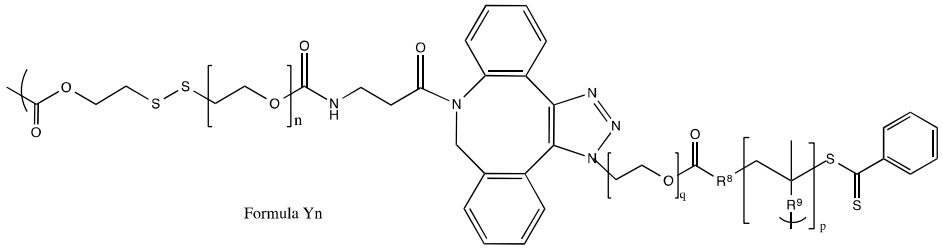
Formula Yk



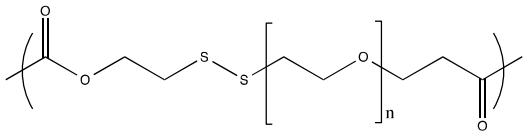
Formula YL



Formula Ym

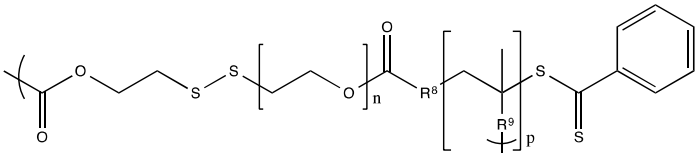


Formula Yn



Formula Yo

and



Formula Yp

where:

the left bracket "(" indicates the bond between X and Y;

the right or bottom bracket and ")" indicates the bond between Y and Z;

n is an integer from 1 to 100;

p is an integer from 2 to 150;

q is an integer from 1 to 44;

R^8 is $–CH_2–$ or $–CH_2-CH_2-C(CH_3)(CN)–$; and

R^9 is a direct bond or $-C(O)-NH-CH_2-CH_2-$.

5. The composition of claim 4 where:

n is 40 to 80;

p is 10 to 100;

q is 3 to 20;

R^8 is $–CH_2-CH_2-C(CH_3)(CN)–$; and

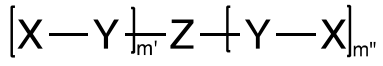
when R^9 is -C(O)-NH-CH2-CH2-, Z is galactose or N-acetylgalactosamine conjugated at its C1.

6. The composition of claim 4 or 5 where Y comprises Formula Ya, Formula Yb, Formula Yc, Formula Ym, Formula Yn or Formula Yp.

7. The composition of claim 4 or 5 where Y comprises Formula Ym.

8. The composition of claim 4 or 5 where Y comprises Formula Yc.

9. A composition comprising a compound of Formula 2:



Formula 2

where:

m' is zero or an integer from 1 to 10, m" is zero or an integer from 1 to 10, and the sum of m' + m" is an integer from 1 to 10 but is at least 1;

each X comprises an antigen which induces an unwanted immune response, or a tolerogenic portion thereof;

wherein X comprises:

a self-antigen;

a transplant antigen,

a food, fungus, dust, cat, mouse, dog, horse, or plant antigen, or

a therapeutic agent that is not naturally occurring;

each Y comprises a linker moiety or a direct bond; and

Z comprises a liver-targeting moeity;

wherein Z comprises one or more of galactose, galactosamine, or N-acetylgalactosamine,

provided that X is not interferon, Ribavirin, Nexavar/ Sorafenib, Erbitus/Cetuximab, bevacizumab or Herceptin/trastuzumab when m'+m" equals 1.

10. The composition of claim 9 where X:

comprises one or more of insulin, proinsulin, preproinsulin, glutamic acid decarboxylase-65 GAD-67, glucose-6 phosphatase 2, insulinoma-associated protein 2, insulinoma-associated protein 2β, ICA69, ICA12, carboxypeptidase H, Imogen 38, GLIMA 38, chromogranin-A, HSP-60, caboxypeptidase E, peripherin, glucose transporter 2, hepatocarcinoma-intestine-pancreas/pancreatic associated protein, S100β, glial fibrillary acidic protein, regenerating gene II, pancreatic duodenal homeobox 1, dystrophia myotonica kinase, islet-specific glucose-6-phosphatase catalytic subunit-related protein, and SST G-protein coupled receptors 1-5;

comprises two or more of myelin basic protein, myelin oligodendrocyte glycoprotein, myelin proteolipid protein, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, and SEQ ID NO:17; or

comprises two or more of SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, and SEQ ID NO:27.

11. The composition of claim 9 where Y is a linker having an immunoproteosome cleavage site.

12. The compositions of claim 9 where X comprises:

a foreign transplant antigen against which transplant recipients develop an unwanted immune response;

a foreign food, fungus, dust, cat, mouse, dog, horse, or plant antigen against which patients develop an unwanted immune response;

a foreign therapeutic agent that is not naturally occurring against which patients develop an unwanted immune response; or

a synthetic self-antigen against the endogenous version of which patients develop an unwanted immune response,

or a tolerogenic portion of any of the foregoing.

13. Use of a composition comprising a compound of Formula 1 in the manufacture of a medicament for treating an unwanted immune response against an antigen, the composition comprising an effective amount of the composition comprising the compound of Formula 1:

$$X\left[Y-Z\right]_m$$

Formula 1

where:

m is an integer from 1 to 100;

X comprises an antigen which induces an unwanted immune response, or a tolerogenic portion thereof;

wherein X comprises:

a self-antigen;

a transplant antigen,

a food, fungus, dust, cat, mouse, dog, horse, or plant antigen, or

a therapeutic agent that is not naturally occurring;

Y comprises a linker moiety; and

Z comprises a liver-targeting moiety;

wherein Z comprises galactose; galactosamine, or N-acetylgalactosamine.

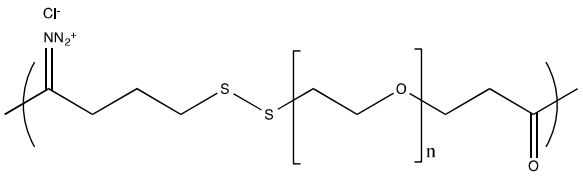
14. The use of claim 13 where:

X comprises an antigen against which a patient develops an unwanted immune response, or a tolerogenic portion thereof; and

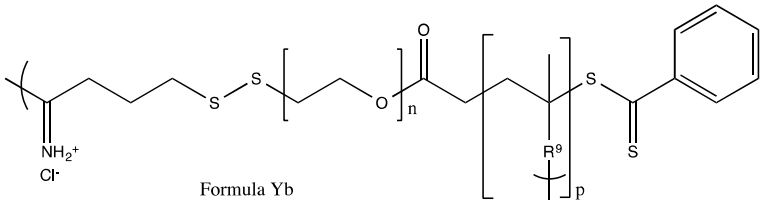
Y comprises:

a disulfanyl ethyl ester; and/or

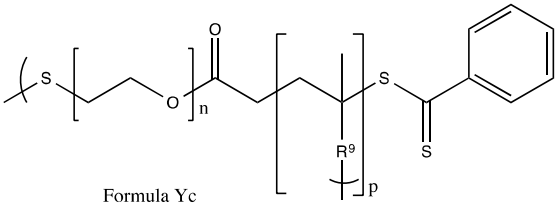
a structure represented by one of Formulae Ya to Yp:



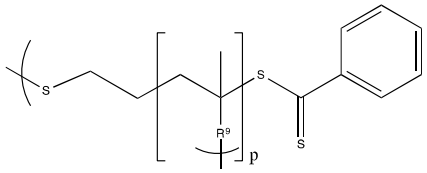
Formula Ya



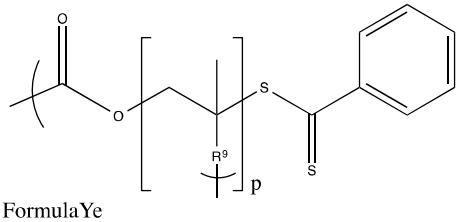
Formula Yb



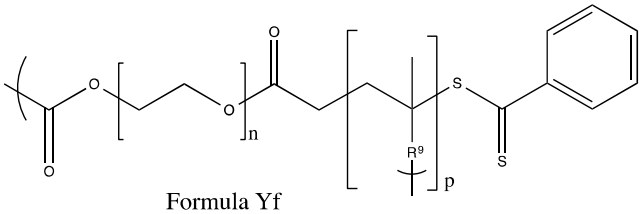
Formula Yc



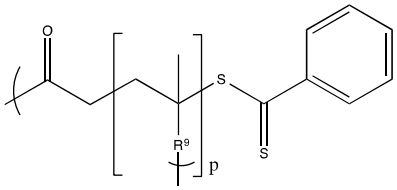
Formula Yd



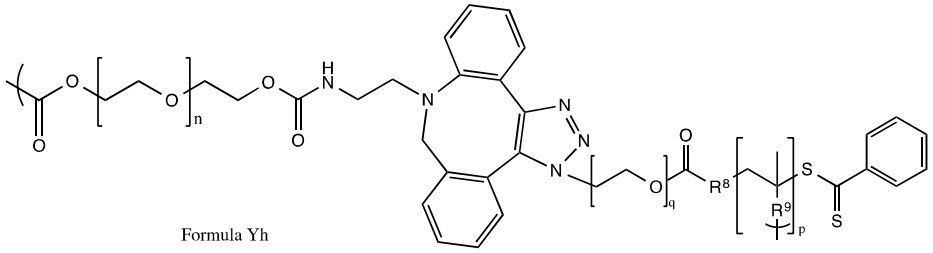
FormulaYe



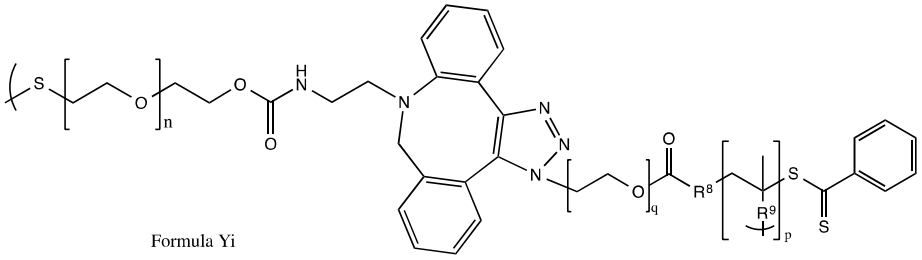
Formula Yf



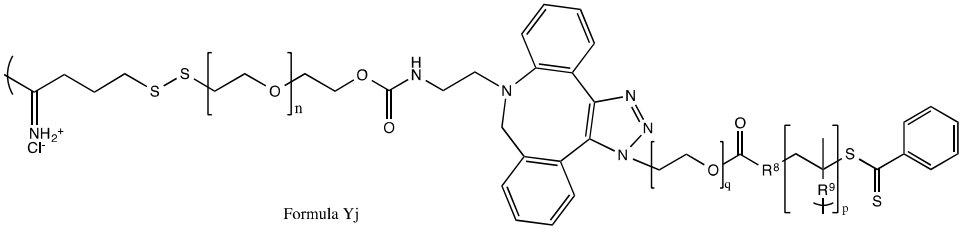
Formula Yg



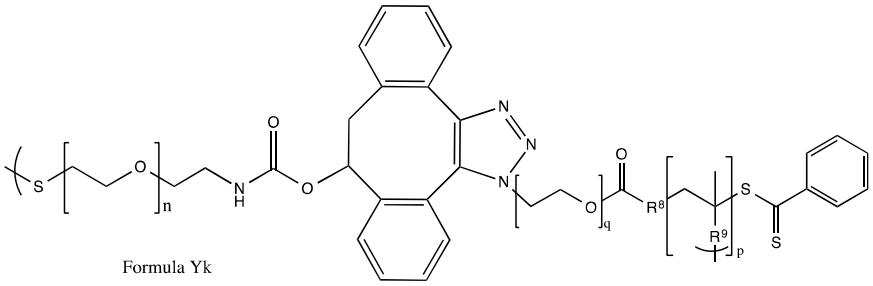
Formula Yh



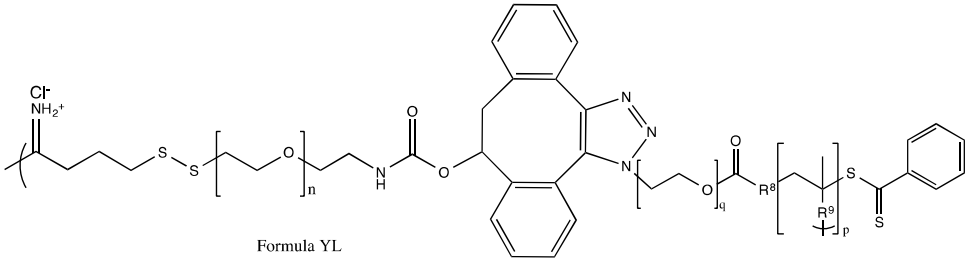
Formula Yi



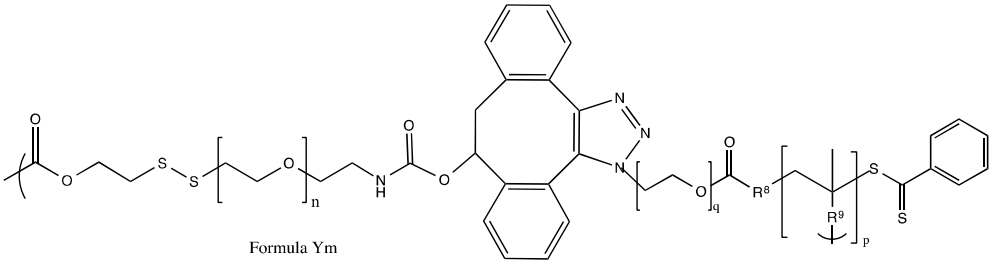
Formula Yj



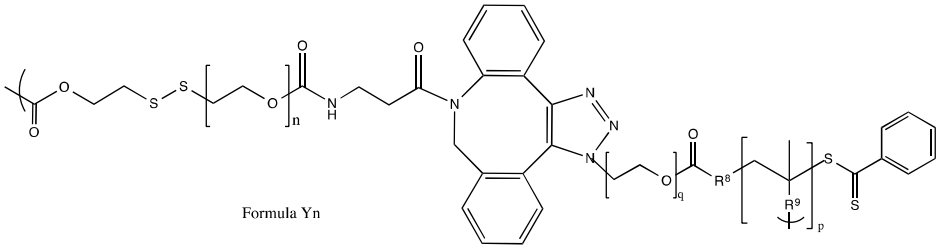
Formula Yk



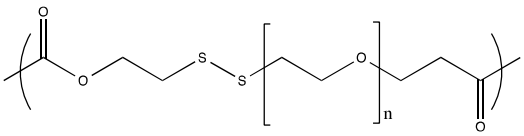
Formula YL



Formula Ym

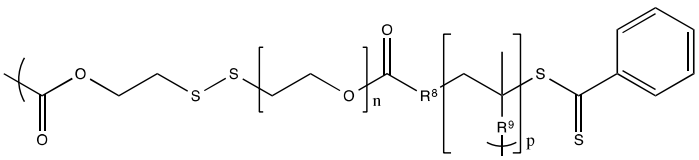


Formula Yn



Formula Yo

and



Formula Yp

where:

the left bracket “(“ indicates the bond between X and Y;

the right or bottom bracket and “)” indicates the bond between Y and Z;

n is an integer from 1 to 100;

p is an integer from 2 to 150;

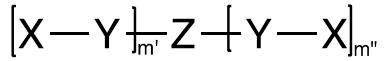
q is an integer from 1 to 44;

R^8 is $–CH_2–$ or $–CH_2\text{-}CH_2\text{-}C(CH_3)(CN)–$; and

R^9 is a direct bond or $\text{-}C(O)\text{-}NH\text{-}CH_2\text{-}CH_2\text{-}$.

15. The use of claim 14 wherein the composition is to be administered for tolerization of the patient with respect to antigen moiety X.

16. Use of a composition comprising a compound of Formula 2 in the manufacture of a medicament for treating an unwanted immune response against an antigen, the composition comprising an effective amount of the composition comprising Formula 2:



Formula 2

where:

m' is zero or an integer from 1 to 10, m" is zero or an integer from 1 to 10, and the sum of m' + m" is an integer from t 1 to 10 but is at least 1;

each X is an antigen which induces an unwanted immune response, or a tolerogenic portion thereof;

wherein X comprises:

a self-antigen;

a transplant antigent,

a food, fungus, dust, cat, mouse, dog, horse, or plant antigen, or

a therapeutic agent that is not naturally occurring;

each Y is a linker moiety or a direct bond; and

Z comprises a liver-targeting moiety;

wherein Z comprises one or more of galactose, galactosamine, or N-acetylgalactosamine.

provided that X is not interferon, Ribavirin, Nexavar/ Sorafenib, Erbitus/Cetuximab, bevacizumab or Herceptin/trastuzumab when m'+m" equals 1.

17. The use of claim 16 wherein the composition is to be administered for tolerization of the patient with respect to antigen moiety X.

18. The use of claim 16 where each X is selected from a group that comprises related antigens which induce an unwanted immune response or a group of tolerogenic fragments thereof.

19. The use of claim 16 where X:

comprises one or more of insulin, proinsulin, preproinsulin, glutamic acid decarboxylase-65 GAD-67, glucose-6 phosphatase 2, insulinoma-associated protein 2, insulinoma-associated protein 2β, ICA69, ICA12, carboxypeptidase H, Imogen 38, GLIMA 38, chromogranin-A, HSP-60, caboxypeptidase E, peripherin, glucose transporter 2,

hepatocarcinoma-intestine-pancreas/pancreatic associated protein, S100β, glial fibrillary acidic protein, regenerating gene II, pancreatic duodenal homeobox 1, dystrophia myotonica kinase, islet-specific glucose-6-phosphatase catalytic subunit-related protein, and SST G-protein coupled receptors 1-5;

comprises two or more of myelin basic protein, myelin oligodendrocyte glycoprotein, myelin proteolipid protein, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, and SEQ ID NO:17; or

comprises two or more of SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, and SEQ ID NO:27.

20. Use of the composition of any one of claims, 1-12 in the preparation of a medicament for tolerization of a patient with respect to X, wherein X comprises an antigen against which a patient develops an unwanted immune response, or a tolerogenic portion thereof.

21. Use of the composition of any one of claims 1-12 in the preparation of a medicament for tolerization of a patient with respect to antigen moiety X.

22. A composition according to any one of claims 1-12, wherein X is an antigen associated with celiac disease.

23. A composition according to any one of claims 1-12, wherein X is an antigen associated with Type I diabetes.

24. A composition according to any one of claims 1-12, wherein X is an antigen associated with multiple sclerosis.

25. A composition according to any one of claims 1-12, wherein X is an antigen associated with an adverse reaction to a therapeutic agent.

26. A composition according to any one of claims 1-12, wherein X is an antigen associated with an adverse reaction to a tissue transplant.

27. A composition according to any one of claims 1-12, where X is selected from the group consisting of myelin oligodendrocyte glycoprotein, myelin proteolipid protein, myelin basic protein, a portion of any of said antigens, and a mimetic of any of said antigens and wherein the unwanted immune response is associated with multiple sclerosis.

28. A composition according to any one of claims 1-12, where X is a synthetic self-antigen and the unwanted immune response is an autoimmune response.

29. A composition according to any one of claims 1-12, where X is a food antigen selected from

the group consisting of: conarachin (Ara h 1), allergen II (Ara h 2), arachis agglutinin, conglutin (Ara h 6), a-lactalbumin (ALA), lactotransferrin, Pen a 1 allergen (Pen a 1), allergen Pen m 2 (Pen m 2), tropomyosin fast isoform, high molecular weight glutenin, low molecular weight glutenin, alpha-gliadin, gamma-gliadin, omega-gliadin, hordein, secalin, avenin, a portion of any of said antigens, and a mimetic of any of said antigens.

30. A composition according to any one of claims 1-12, where X is selected from the group consisting of insulin, proinsulin, preproinsulin, insulinoma-associated protein 2, insulinoma-associated protein 2β, a portion of any of said antigens, and a mimetic of any of said antigens and wherein the unwanted immune response is associated with type 1 diabetes mellitus.

31. A composition according to any one of claims 1-12, where X comprises a foreign transplant antigen against which transplant recipients develop an unwanted immune response or a tolerogenic portion thereof.

32. A composition according to any one of claims 1-12, where X is a therapeutic agent selected from the group consisting of Factor VIII and Factor IX.

33. A composition according to any one of claims 1-12, where X is a therapeutic agent selected from the group consisting of asparaginase and uricase.

34. The composition of claim 4 where:
Y is Y_c;
R^8 is $-CH_2-CH_2-C(CH_3)(CN)-$;
R^9 is $-C(O)-NH-CH_2-CH_2-$; and
Z is N-acetylgalactosamine.

35. The composition of claim 4 where:
Y is Y_m;
R^8 is $-CH_2-CH_2-C(CH_3)(CN)-$;
R^9 is $-C(O)-NH-CH_2-CH_2-$; and
Z is N-acetylgalactosamine.

36. The composition of claim 13, wherein the unwanted immune response is associated with multiple sclerosis.

37. The composition of claim 13, wherein the unwanted immune response is associated with transplant rejection.

38. A composition according to any one of claims 1-12, where Z comprises a beta anomer.

39. A composition according to any one of claims 1-12, where X comprises one or more of conarachin (Ara h 1), allergen II (Ara h 2), arachis agglutinin, conglutin (Ara h 6), 31 kda major allergen/disease resistance protein homolog (Mal d 2), lipid transfer protein precursor (Mal d 3), major allergen Mal d 1.03D (Mal d 1), a-lactalbumin (ALA), lactotransferrin, actinidin (Act c 1, Act d 1), phytocystatin, thaumatin-like protein (Act d 2), kiwellin (Act d 5), ovomucoid, ovalbumin, ovotransferrin, and lysozyme, livetin, apovitillin, vosvetin, 2S albumin (Sin a 1), 1 lS globulin (Sin a 2), lipid transfer protein (Sin a 3), profilin (Sin a 4), profilin (Api g 4), high molecular weight glycoprotein (Api g 5), Pen a 1 allergen (Pen a 1), allergen Pen m 2 (Pen m 2), tropomyosin fast isoform, high molecular weight glutenin, low molecular weight glutenin, alpha-, gamma- and omega-gliadin, hordein, secalin, avenin, major strawberry allergy Fra a 1-E (Fra a 1), profilin (Mus xp 1), a portion of any of said antigens, and a mimetic of any of said antigens.

40. A composition according to any one of claims 1-12, where X comprises one or more of high molecular weight glutenin, low molecular weight glutenin, alpha-, gamma- and omega-gliadin, hordein, secalin, avenin, a portion of any of said antigens, and a mimetic of any of said antigens.

41. A composition according to any one of claims 1-12, where X comprises one or more of gliadin, a portion of gliadin, and a mimetic of any of said antigens.

42. A composition according to any one of claims 1-12, where X comprises one or more of insulin, proinsulin, preproinsulin, glutamic acid decarboxylase-65 (GAD-65), GAD-67, insulinoma associated protein 2 (IA-2), and insulinoma-associated protein 2β (IA-2β), ICA69, ICA12 (SOX-13), carboxypeptidase H, Imogen 38, GLIMA 38, chromogranin- A, HSP-60, caboxypeptidase E, peripherin, glucose transporter 2, hepatocarcinoma-intestinepancreas/pancreatic associated protein, S100β, glial fibrillary acidic protein, regenerating gene II, pancreatic duodenal homeobox 1, dystrophia myotonica kinase, islet-specific glucose-6- phosphatase catalytic subunit-related protein, SST G-protein coupled receptors 1-5, and a portion of any of said antigens, and a mimetic of any of said antigens.

43. A composition according to any one of claims 1-12, where X comprises one or more of Abciximab, Adalimumab, Agalsidase alfa, Agalsidase beta, Aldeslukin, Alglucosidase alfa, Factor VIII, Factor IX, Infliximab, L-asparaginase, Laronidase, Natalizumab, Octreotide, Phenylalanine ammonia-lyase (PAL), or Rasburicase (uricase), a portion of any of said antigens, and a mimetic of any of said antigens.

44. A composition according to any one of claims 1-12, where X comprises one or more subunits of the MHC class I and MHC class II haplotype proteins, and minor blood group antigens RhCE, Kell, Kidd, Duffy and Ss.

45. A composition according to any one of claims 1-12, where X comprises one or more of insulin,

proinsulin, preproinsulin, a tolerogenic portion of any of said antigens, or a mimetic of any one of said antigens.

46. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising an amino acid sequence of SEQ ID NO. 24 or SEQ ID NO. 25.

47. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising a portion of SEQ. ID. NO. 5.

48. The composition of Claim 48, wherein X comprises a polypeptide comprising an amino acid sequence comprising a portion of SEQ. ID. NO. 5 and one or more of IA-2, a fragment thereof, or a mimotope thereof.

49. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising a portion of SEQ. ID. NO. 8.

50. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising a portion of SEQ. ID. NO. 9.

51. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising a portion of SEQ. ID. NO. 10.

52. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising an amino acid sequence of SEQ ID NO. 11.

53. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising an amino acid sequence of SEQ ID NO. 12.

54. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising an amino acid sequence of SEQ ID NO. 13.

55. A composition according to any one of claims 1-12, where X comprises a polypeptide comprising an amino acid sequence of SEQ ID NO. 14.

56. A composition according to any one of claims 1-12, where X comprises SEQ ID NO. 15.

57. A composition according to any one of claims 1-12, where X comprises SEQ ID NO. 16.

58. A composition according to any one of claims 1-12, where X comprises SEQ ID NO. 17.

59. A composition according to any one of claims 1-12, where X comprises one or both of SEQ ID NO. 15 and SEQ ID NO. 16 and wherein X further comprises SEQ ID NO. 12.

60. A composition according to any one of claims 1-12, where X is associated with an autoimmune disease selected from the group consisting of Type I diabetes, multiple sclerosis, rheumatoid arthritis, vitiligo, uveitis, pemphis vulgaris and neuromyelitis optica.

61. A composition according to any one of claims 1-12, where X comprises one or more of fibrinogen, vimentin, collagen type II, alpha enolase, Pmel17, tyrosinase, retinal arrestin, interphotoreceptor retinoid-binding protein (IRBP), desmoglein 3, 1 and 4, pemphaxin, desmocollins, plakoglobin, perplakin, desmoplakins, acetylcholine receptor, aquaporin-4, a fragment thereof, or a mimotope thereof.