WHAT IS CLAIMED IS:

1. A therapeutic nanoparticle comprising:

about 0.05 to about 30 weight percent of a substantially hydrophobic acid;

about 0.2 to about 25 weight percent of a therapeutic agent; wherein the pK_a of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

about 50 to about 99.75 weight percent of a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combination, wherein the therapeutic nanoparticle comprises about 10 to about 30 weight percent poly(ethylene)glycol, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

2. The therapeutic nanoparticle according to claim 1 comprising:

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of about 1:7 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea:PLA-PEG.

3. The therapeutic nanoparticle according to claim 1 comprising:

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of about 1:14 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea:PLA-PEG.

4. The therapeutic nanoparticle according to claim 1 comprising:

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of about 1:5 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea:PLA-PEG.

5. A therapeutic nanoparticle comprising:

about 0.2 to about 25 weight percent of a therapeutic agent;

a substantially hydrophobic acid, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent ranges from about 0.25:1 to about 2:1 and wherein the pKa of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

about 50 to about 99.75 weight percent of a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combination, wherein the therapeutic nanoparticle comprises about 10 to about 30 weight percent poly(ethylene)glycol, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

6. A therapeutic nanoparticle comprising:

a substantially hydrophobic acid;

a therapeutic agent; wherein the pK_a of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combination thereof, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

7. A therapeutic nanoparticle comprising:

a therapeutic agent;

a substantially hydrophobic acid, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent ranges from about 0.25:1 to about 2:1 and wherein

the pKa of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combination thereof, and, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

8. The therapeutic nanoparticle of claim 5 or 7, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent is about 0.5:1 to about 1.5:1.

9. The therapeutic nanoparticle of claim 5 or 7, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent is about 0.25:1 to about 1:1.

10. The therapeutic nanoparticle of claim 5 or 7, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent is about 0.75:1 to about 1.25:1.

11. The therapeutic nanoparticle of any one of claims 1-10, wherein the pK_a of the protonated therapeutic agent is at least about 2.0 pK_a units greater than the pK_a of the hydrophobic acid.

12. The therapeutic nanoparticle of any one of claims 1-10, wherein the pK_a of the protonated therapeutic agent is at least about 4.0 pK_a units greater than the pK_a of the hydrophobic acid.

13. A therapeutic nanoparticle comprising:

a hydrophobic ion-pair comprising a hydrophobic acid and therapeutic agent; wherein the difference between the pKa of the protonated therapeutic agent and the hydrophobic acid is at least about 1.0 pKa units or greater; and

about 50 to about 99.75 weight percent of a diblock poly(lactic) acid-poly(ethylene)glycol copolymer, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a number average molecular weight of about 15 kDa to about 20 kDa poly(lactic acid) and a number average molecular weight of about 4 kDa to about 6 kDa poly(ethylene)glycol, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-

yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

14. The therapeutic nanoparticle of claim 13, wherein the difference between the pKa of the protonated therapeutic agent and the hydrophobic acid is at least about 2.0 pKa units.

15. The therapeutic nanoparticle of claim 13, wherein the difference between the pKa of the protonated therapeutic agent and the hydrophobic acid is at least about 4.0 pKa units.

16. The therapeutic nanoparticle of any one of claims 1-4, 6, or 11-15, comprising about 0.05 to about 20 weight percent of the hydrophobic acid.

17. The therapeutic nanoparticle of any one of claims 1-16, wherein the substantially hydrophobic acid has a logP ranging from about 2 to about 7.

18. The therapeutic nanoparticle of any one of claims 1-16, wherein the substantially hydrophobic acid has a logP ranging from about 4 to about 8.

19. The therapeutic nanoparticle of any one of claims 1-18, wherein the substantially hydrophobic acid has a pK_a in water from about -1.0 to about 5.0.

20. The therapeutic nanoparticle of any one of claims 1-18, wherein the substantially hydrophobic acid has a pK_a in water from about 2.0 to about 5.0.

21. The therapeutic nanoparticle of any one of claims 1-20, wherein the substantially hydrophobic acid and the therapeutic agent form a hydrophobic ion pair in the therapeutic nanoparticle.

22. The therapeutic nanoparticle of any one of claims 1-21, wherein the hydrophobic acid is a fatty acid.

23. The therapeutic nanoparticle of claim 22, wherein the fatty acid is a saturated fatty acid selected from the group consisting of: caproic acid, enanthic acid, caprylic acid, pelargonic acid, capric acid, undecanoic acid, lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, nonadecylic acid, arachidic

acid, heneicosylic acid, behenic acid, tricosylic acid, lignoceric acid, pentacosylic acid, cerotic acid, heptacosylic acid, montanic acid, nonacosylic acid, melissic acid, henatriacontylic acid, lacceroic acid, psyllic acid, geddic acid, ceroplastic acid, hexatriacontylic acid, and combinations thereof.

24. The therapeutic nanoparticle of claim 22, wherein the fatty acid is an omega-3 fatty acid selected from the group consisting of: hexadecatrienoic acid, alpha-linolenic acid, stearidonic acid, eicosatrienoic acid, eicosatetraenoic acid, eicosapentaenoic acid, heneicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid, tetracosapentaenoic acid, tetracosahexaenoic acid, and combinations thereof.

25. The therapeutic nanoparticle of claim 22, wherein the fatty acid is an omega-6 fatty acid selected from the group consisting of: linoleic acid, gamma-linolenic acid, eicosadienoic acid, dihomo-gamma-linolenic acid, arachidonic acid, docosadienoic acid, adrenic acid, docosapentaenoic acid, tetracosatetraenoic acid, tetracosapentaenoic acid, and combinations thereof.

26. The therapeutic nanoparticle of claim 22, wherein the fatty acid is an omega-9 fatty acid selected from the group consisting of: oleic acid, eicosenoic acid, mead acid, erucic acid, nervonic acid, and combinations thereof.

27. The therapeutic nanoparticle of claim 26, wherein the fatty acid is oleic acid.

28. The therapeutic nanoparticle of claim 27 wherein the weight ratio of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea to oleic acid is about 6:1.

29. The therapeutic nanoparticle of claim 22, wherein the fatty acid is a polyunsaturated fatty acid selected from the group consisting of: rumenic acid, α-calendic acid, β-calendic acid, jacaric acid, α-eleostearic acid, β-eleostearic acid, catalpic acid, punicic acid, rumelenic acid, α-parinaric acid, β-parinaric acid, bosseopentaenoic acid, pinolenic acid, podocarpic acid, and combinations thereof.

30. The therapeutic nanoparticle of any one of claims 1-22, wherein the hydrophobic

acid is a bile acid.

31. The therapeutic nanoparticle of claim 30, wherein the bile acid is selected from the group consisting of chenodeoxycholic acid, ursodeoxycholic acid, deoxycholic acid, hycholic acid, beta-muricholic acid, cholic acid, lithocholic acid, an amino acid-conjugated bile acid, and combinations thereof.

32. The therapeutic nanoparticle of claim 31, wherein the bile acid is cholic acid.

33. The therapeutic nanoparticle of claim 31, wherein the amino acid-conjugated bile acid is a glycine-conjugated bile acid or a taurine-conjugated bile acid.

34. The therapeutic nanoparticle of any one of claims 1-21, wherein the hydrophobic acid is selected from the group consisting of dioctyl sulfosuccinic acid, 1-hydroxy-2-naphthoic acid, dodecylsulfuric acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, pamoic acid, undecanoic acid, and combinations thereof.

35. The therapeutic nanoparticle of claim 34, wherein the hydrophobic acid is pamoic acid.

36. The therapeutic nanoparticle of claim 35 wherein the weight ratio of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea to pamoic acid is about 1.8:1.

37. The therapeutic nanoparticle of any one of claims 1-36, comprising about 1 to about 20 weight percent of the therapeutic agent.

38. The therapeutic nanoparticle of any one of claims 1-36, comprising about 2 to about 20 weight percent of the therapeutic agent.

39. The therapeutic nanoparticle of any one of claims 1-36, comprising about 4 to about 20 weight percent of the therapeutic agent.

40. The therapeutic nanoparticle of any one of claims 1-36, comprising about 5 to about 20 weight percent of the therapeutic agent.

41. The therapeutic nanoparticle of any one of claims 1-36, wherein the hydrophobic acid has a molecular weight of between about 200 Da and about 800 Da.

42. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle substantially retains the therapeutic agent for at least 1 minute when placed in a phosphate buffer solution at 37 °C.

43. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle substantially immediately releases less than about 30% of the therapeutic agent when placed in a phosphate buffer solution at 37 °C.

44. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 10 to about 45% of the therapeutic agent over about 1 hour when placed in a phosphate buffer solution at 37 °C.

45. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 4 hours when placed in a phosphate buffer solution at 37 °C.

46. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 10 hours when placed in a phosphate buffer solution at 37 °C.

47. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 0.01 to about 25% of the therapeutic agent over about 20 hours when placed in a phosphate buffer solution at 37 °C.

48. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 1 to about 40% of the therapeutic agent over about 40 hours when placed in a phosphate buffer solution at 37 °C.

49. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle has a release profile that is substantially the same as a release profile for a control nanoparticle that is substantially the same as the therapeutic nanoparticle except that it does not contain a fatty acid or bile acid.

50. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.6 to about 0.95.

51. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.6 to about 0.8.

52. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.75 to about 0.85.

53. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.7 to about 0.9.

54. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 10 to about 25 weight percent poly(ethylene)glycol.

55. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 10 to about 20 weight percent poly(ethylene)glycol.

56. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 15 to about 25 weight percent poly(ethylene)glycol.

57. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 20 to about 30 weight percent poly(ethylene)glycol.

58. The therapeutic nanoparticle of any one of claims 1-57, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a number average molecular weight of about 15 kDa to about 20 kDa poly(lactic acid) and a number average molecular weight of about 4 kDa to about 6 kDa poly(ethylene)glycol.

59. The therapeutic nanoparticle of any one of claims 1-58, further comprising about 0.2 to about 30 weight percent poly(lactic) acid-poly(ethylene)glycol copolymer functionalized

with a targeting ligand.

60. The therapeutic nanoparticle of any one of claims 1-58, further comprising about 0.2 to about 30 weight percent poly(lactic) acid-co-poly(glycolic) acid-poly(ethylene)glycol copolymer functionalized with a targeting ligand.

61. The therapeutic nanoparticle of claim 59 or 60, wherein the targeting ligand is covalently bound to the poly(ethylene)glycol.

62. The therapeutic nanoparticle of any one of claims 1-61, wherein the hydrophobic acid is a polyelectrolyte.

63. The therapeutic nanoparticle of claim 62, wherein the polyelectrolyte is selected from the group consisting of a poly(styrene sulfonic acid), polypolyacrylic acid, and polymethacrylic acid.

64. The therapeutic nanoparticle of any one of claims 1-63, wherein the substantially hydrophobic acid is a mixture of two or more substantially hydrophobic acids.

65. The therapeutic nanoparticle of claim 64, comprising a mixture of two substantially hydrophobic acids.

66. The therapeutic nanoparticle of claim 65, wherein the two substantially hydrophobic acids are oleic acid and cholic acid.

67. The therapeutic nanoparticle of claim 64, comprising a mixture of three substantially hydrophobic acids.

68. The therapeutic nanoparticle of claim 64, comprising a mixture of four substantially hydrophobic acids.

69. The therapeutic nanoparticle of claim 64, comprising a mixture of five substantially hydrophobic acids.

70. A therapeutic nanoparticle prepared by the process comprising the steps of:

emulsification of a first organic phase comprising a first polymer, a therapeutic

agent, and a substantially hydrophobic acid, thereby forming an emulsion phase;

quenching of the emulsion phase thereby forming a quenched phase; and

filtration of the quenched phase to recover the therapeutic nanoparticles, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

71. The therapeutic nanoparticle of claim 70, wherein the hydrophobic acid is a fatty acid.

72. The therapeutic nanoparticle of claim 71, wherein the fatty acid is a saturated fatty acid selected from the group consisting of: caproic acid, enanthic acid, caprylic acid, pelargonic acid, capric acid, undecanoic acid, lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, nonadecylic acid, arachidic acid, heneicosylic acid, behenic acid, tricosylic acid, lignoceric acid, pentacosylic acid, cerotic acid, heptacosylic acid, montanic acid, nonacosylic acid, melissic acid, henatriacontylic acid, lacceroic acid, psyllic acid, geddic acid, ceroplastic acid, hexatriacontylic acid, and combinations thereof.

73. The therapeutic nanoparticle of claim 71, wherein the fatty acid is an omega-3 fatty acid selected from the group consisting of: hexadecatrienoic acid, alpha-linolenic acid, stearidonic acid, eicosatrienoic acid, eicosatetraenoic acid, eicosapentaenoic acid, heneicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid, tetracosapentaenoic acid, tetracosahexaenoic acid, and combinations thereof.

74. The therapeutic nanoparticle of claim 71, wherein the fatty acid is an omega-6 fatty acid selected from the group consisting of: linoleic acid, gamma-linolenic acid, eicosadienoic acid, dihomo-gamma-linolenic acid, arachidonic acid, docosadienoic acid, adrenic acid, docosapentaenoic acid, tetracosatetraenoic acid, tetracosapentaenoic acid, and combinations thereof.

75. The therapeutic nanoparticle of claim 71, wherein the fatty acid is an omega-9 fatty acid selected from the group consisting of: oleic acid, eicosenoic acid, mead acid, erucic

acid, nervonic acid, and combinations thereof.

76. The therapeutic nanoparticle of claim 75, wherein the fatty acid is oleic acid.

77. The therapeutic nanoparticle of claim 71, wherein the fatty acid is a polyunsaturated fatty acid selected from the group consisting of: rumenic acid, α-calendic acid, β-calendic acid, jacaric acid, α-eleostearic acid, β-eleostearic acid, catalpic acid, punicic acid, rumelenic acid, α-parinaric acid, β-parinaric acid, bosseopentaenoic acid, pinolenic acid, podocarpic acid, and combinations thereof.

78. The therapeutic nanoparticle of any one of claims 70, wherein the hydrophobic acid is a bile acid.

79. The therapeutic nanoparticle of claim 78, wherein the bile acid is selected from the group consisting of chenodcoxycholic acid, ursodcoxycholic acid, dcoxycholic acid, hycholic acid, beta-muricholic acid, cholic acid, lithocholic acid, an amino acid-conjugated bile acid, and combinations thereof.

80. The therapeutic nanoparticle of claim 79, wherein the bile acid is cholic acid.

81. The therapeutic nanoparticle of claim 79, wherein the amino acid-conjugated bile acid is a glycine-conjugated bile acid or a taurine-conjugated bile acid.

82. The therapeutic nanoparticle of any one of claims 70, wherein the hydrophobic acid is selected from the group consisting of dioctyl sulfosuccinic acid, 1-hydroxy-2-naphthoic acid, dodecylsulfuric acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, pamoic acid, undecanoic acid, and combinations thereof.

83. The therapeutic nanoparticle of claim 82, wherein the hydrophobic acid is pamoic acid.

84. The therapeutic nanoparticle of any one of claims 70-83, wherein the hydrophobic acid has a molecular weight of between about 200 Da and about 800 Da.

85. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic

nanoparticle substantially retains the therapeutic agent for at least 1 minute when placed in a phosphate buffer solution at 37 °C.

86. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle substantially immediately releases less than about 30% of the therapeutic agent when placed in a phosphate buffer solution at 37 °C.

87. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 10 to about 45% of the therapeutic agent over about 1 hour when placed in a phosphate buffer solution at 37 °C.

88. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 4 hours when placed in a phosphate buffer solution at 37 °C.

89. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 10 hours when placed in a phosphate buffer solution at 37 °C.

90. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 0.01 to about 25% of the therapeutic agent over about 20 hours when placed in a phosphate buffer solution at 37 °C.

91. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 1 to about 40% of the therapeutic agent over about 40 hours when placed in a phosphate buffer solution at 37 °C.

92. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle has a release profile that is substantially the same as a release profile for a control nanoparticle that is substantially the same as the therapeutic nanoparticle except that it does not contain a fatty acid or bile acid.

93. The therapeutic nanoparticle of any one of claims 70-92, wherein the first polymer is poly(lactic) acid-poly(ethylene)glycol copolymer.

94. The therapeutic nanoparticle of any one of claims 70-92, wherein the first polymer is poly(lactic) acid-co-poly(glycolic) acid-poly(ethylene)glycol copolymer.

95. The therapeutic nanoparticle of any one of claims 70-94, wherein the substantially hydrophobic acid is a mixture of two or more substantially hydrophobic acids.

96. The therapeutic nanoparticle of claim 95, comprising a mixture of two substantially hydrophobic acids.

97. The therapeutic nanoparticle of claim 95, comprising a mixture of three substantially hydrophobic acids.

98. The therapeutic nanoparticle of claim 95, comprising a mixture of four substantially hydrophobic acids.

99. The therapeutic nanoparticle of claim 95, comprising a mixture of five substantially hydrophobic acids.

100. The therapeutic nanoparticle of any of claims 1, 5-93, or 95-99 wherein the polymer is PLA-PEG and the mole ratio of PLA-PEG is 5:1.

101. A therapeutic nanoparticle prepared by the process comprising the steps of:

combining a first organic phase with a first aqueous solution to form a second phase;

emulsifying the second phase to form an emulsion phase, wherein the emulsion phase comprises a first polymer, therapeutic agent, and a substantially hydrophobic acid;

quenching of the emulsion phase thereby forming a quenched phase; and

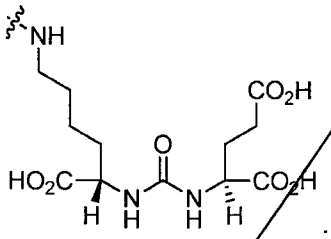
filtering the quenched phase to recover the therapeutic nanoparticles, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, the first organic phase comprises the therapeutic agent and pamoic acid in a weight ratio of therapeutic agent to pamoic acid of about 11:1 and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of therapeutic agent to PLA-PEG of about 1:3 in an organic solvent comprising of benzyl alcohol and ethyl acetate in a weight ratio of benzyl alcohol to ethyl acetate of about 1.25 and the first aqueous solution comprises a polyoxyethylene (100) stearyl ether dissolved in benzyl alcohol in a

weight ratio of 0.005:1 and combining the first organic phase and the first aqueous phase in a weight ratio of about 1:5 to form a second phase and emulsifying the second phase formed therefrom and quenching the emulsion phase with 0.1 M citric acid in water solution at pH 4.5 and concentrating the resulting product.

102. A therapeutic nanoparticle of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or pharmaceutically acceptable salt thereof.

103. A therapeutic nanoparticle comprising of a therapeutic agent or a pharmaceutically acceptable salt thereof and a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combination thereof, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

104. The therapeutic nanoparticle of any of claims 1-69, 102, or 103, wherein a targeting ligand is additionally present and is PLA-PEG-GL, wherein GL has the following structure:



105. The therapeutic nanoparticle according to any one of claims 1-69 or 102-104, further comprising a solubilizer.

106. The therapeutic nanoparticle according to claim 105, wherein the solubilizer is polysorbate 80.

107. The therapeutic nanoparticle of claim 105, wherein the solubilizer is polyoxyethylene (100) stearyl ether.

108. The therapeutic nanoparticle of any one of claims 1-107, wherein the therapeutic

agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea.

109. A pharmaceutical composition comprising a therapeutic nanoparticle of any of claims 1-108 and a pharmaceutically acceptable excipient.

110. The pharmaceutical composition of claim 109 comprising a plurality of therapeutic nanoparticles.

111. The pharmaceutical composition of claim 109 or 110, further comprising a saccharide.

112. The pharmaceutical composition of any one of claims 109-111, further comprising a cyclodextrin.

113. The pharmaceutical composition of claims 111 or 112, wherein the saccharide is a disaccharide selected from the group consisting of sucrose, trehalose, and a mixture thereof.

114. A method of treating cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a therapeutic nanoparticle of any one of claims 1-108 or a pharmaceutical composition of any one of claims 109-113.

115. The method of claim 114, wherein the cancer is chronic myelogenous leukemia.

116. The method of claim 114, wherein the cancer is gastrointestinal stromal tumor.

117. The method of claim 114, wherein the cancer is selected from the group consisting of chronic myelomonocytic leukemia, hypereosinophilic syndrome, renal cell carcinoma, hepatocellular carcinoma, Philadelphia chromosome positive acute lymphoblastic leukemia, non-small cell lung cancer, pancreatic cancer, breast cancer, a solid tumor, head and neck cancer and mantle cell lymphoma.

118. The method of claim 117, wherein the cancer is breast cancer.

119. A process for preparing a therapeutic nanoparticle, comprising the steps of:

combining a first organic phase with a first aqueous solution to form a second phase;

emulsifying the second phase to form an emulsion phase, wherein the emulsion phase comprises a first polymer, therapeutic agent, and a substantially hydrophobic acid;

quenching of the emulsion phase thereby forming a quenched phase; and

filtering the quenched phase to recover the therapeutic nanoparticles, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

120. The process of claim 119, further comprising combining the therapeutic agent and the substantially hydrophobic acid in the second phase prior to emulsifying the second phase.

121. The process of claim 120, wherein the therapeutic agent and the substantially hydrophobic acid form a hydrophobic ion pair prior to emulsifying the second phase.

122. The process of claim 120, wherein the therapeutic agent and the substantially hydrophobic acid form a hydrophobic ion pair prior during emulsification of the second phase.

123. The process of claim 119, further comprising combining the therapeutic agent and the substantially hydrophobic acid in the second phase substantially concurrently with emulsifying the second phase.

124. The process of claim 119, wherein the first organic phase comprises the therapeutic agent and the first aqueous solution comprises the substantially hydrophobic acid.

125. The process of any one of claims 119-124, wherein the therapeutic agent, when protonated, has a first pK_a, the substantially hydrophobic acid has a second pK_a, and the emulsion phase is quenched with an aqueous solution having a pH equal to a pK_a unit between the first pK_a and the second pK_a.

126. The process of claim 125, wherein the quenched phase has a pH equal to a pK_a unit between the first pK_a and the second pK_a.

127. The process of any one of claims 119-126, wherein the therapeutic agent, when

protonated, has a first pK_a, the substantially hydrophobic acid has a second pK_a, and the first aqueous solution has a pH equal to a pK_a unit between the first pK_a and the second pK_a.

128. The process of any one of claims 125-127, wherein the pH is equal to a pK_a unit that is about equidistant between the first pK_a and the second pK_a.

129. The process of any one of claims 119-128, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea.

CLAIMS

1. A therapeutic nanoparticle comprising:

about 0.05 to about 30 weight percent of a substantially hydrophobic acid;

about 0.2 to about 25 weight percent of a therapeutic agent; wherein the pK_a of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

about 50 to about 99.75 weight percent of a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combinations thereof, wherein the therapeutic nanoparticle comprises about 10 to about 30 weight percent poly(ethylene)glycol, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

2. The therapeutic nanoparticle according to claim 1 comprising:

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of about 1:7 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea:PLA-PEG.

3. The therapeutic nanoparticle according to claim 1 comprising:

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of about 1:14 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea:PLA-PEG.

4. The therapeutic nanoparticle according to claim 1 comprising:

1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea;

and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of about 1:5 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea:PLA-PEG.

5. A therapeutic nanoparticle comprising:

about 0.2 to about 25 weight percent of a therapeutic agent;

a substantially hydrophobic acid, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent ranges from about 0.25:1 to about 2:1 and wherein the pKa of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

about 50 to about 99.75 weight percent of a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combinations thereof, wherein the therapeutic nanoparticle comprises about 10 to about 30 weight percent poly(ethylene)glycol, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

6. A therapeutic nanoparticle comprising:

a substantially hydrophobic acid;

a therapeutic agent; wherein the pK_a of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combinations thereof, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

7. A therapeutic nanoparticle comprising:

a therapeutic agent;

a substantially hydrophobic acid, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent ranges from about 0.25:1 to about 2:1 and wherein

the pKa of the protonated therapeutic agent is at least about 1.0 pK_a units greater than the pK_a of the hydrophobic acid; and

a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combinations thereof, and, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

8. The therapeutic nanoparticle of claim 5 or 7, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent is about 0.5:1 to about 1.5:1.

9. The therapeutic nanoparticle of claim 5 or 7, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent is about 0.25:1 to about 1:1.

10. The therapeutic nanoparticle of claim 5 or 7, wherein the molar ratio of the substantially hydrophobic acid to the therapeutic agent is about 0.75:1 to about 1.25:1.

11. The therapeutic nanoparticle of any one of claims 1-10, wherein the pK_a of the protonated therapeutic agent is at least about 2.0 pK_a units greater than the pK_a of the hydrophobic acid.

12. The therapeutic nanoparticle of any one of claims 1-10, wherein the pK_a of the protonated therapeutic agent is at least about 4.0 pK_a units greater than the pK_a of the hydrophobic acid.

13. A therapeutic nanoparticle comprising:

a hydrophobic ion-pair comprising a hydrophobic acid and therapeutic agent; wherein the difference between the pKa of the protonated therapeutic agent and the hydrophobic acid is at least about 1.0 pKa units or greater; and

about 50 to about 99.75 weight percent of a diblock poly(lactic) acid-poly(ethylene)glycol copolymer, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a number average molecular weight of about 15 kDa to about 20 kDa poly(lactic acid) and a number average molecular weight of about 4 kDa to about 6 kDa poly(ethylene)glycol, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-

yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

14. The therapeutic nanoparticle of claim 13, wherein the difference between the pKa of the protonated therapeutic agent and the hydrophobic acid is at least about 2.0 pKa units.

15. The therapeutic nanoparticle of claim 13, wherein the difference between the pKa of the protonated therapeutic agent and the hydrophobic acid is at least about 4.0 pKa units.

16. The therapeutic nanoparticle of any one of claims 1-4, 6, or 11-15, comprising about 0.05 to about 20 weight percent of the hydrophobic acid.

17. The therapeutic nanoparticle of any one of claims 1-16, wherein the substantially hydrophobic acid has a logP ranging from about 2 to about 7.

18. The therapeutic nanoparticle of any one of claims 1-16, wherein the substantially hydrophobic acid has a logP ranging from about 4 to about 8.

19. The therapeutic nanoparticle of any one of claims 1-18, wherein the substantially hydrophobic acid has a pK_a in water from about -1.0 to about 5.0.

20. The therapeutic nanoparticle of any one of claims 1-18, wherein the substantially hydrophobic acid has a pK_a in water from about 2.0 to about 5.0.

21. The therapeutic nanoparticle of any one of claims 1-20, wherein the substantially hydrophobic acid and the therapeutic agent form a hydrophobic ion pair in the therapeutic nanoparticle.

22. The therapeutic nanoparticle of any one of claims 1-21, wherein the hydrophobic acid is a fatty acid.

23. The therapeutic nanoparticle of claim 22, wherein the fatty acid is a saturated fatty acid selected from the group consisting of: caproic acid, enanthic acid, caprylic acid, pelargonic acid, capric acid, undecanoic acid, lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, nonadecylic acid, arachidic

acid, heneicosylic acid, behenic acid, tricosylic acid, lignoceric acid, pentacosylic acid, cerotic acid, heptacosylic acid, montanic acid, nonacosylic acid, melissic acid, henatriacontylic acid, lacceroic acid, psyllic acid, geddic acid, ceroplastic acid, hexatriacontylic acid, and combinations thereof.

24. The therapeutic nanoparticle of claim 22, wherein the fatty acid is an omega-3 fatty acid selected from the group consisting of: hexadecatrienoic acid, alpha-linolenic acid, stearidonic acid, eicosatrienoic acid, eicosatetraenoic acid, eicosapentaenoic acid, heneicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid, tetracosapentaenoic acid, tetracosahexaenoic acid, and combinations thereof.

25. The therapeutic nanoparticle of claim 22, wherein the fatty acid is an omega-6 fatty acid selected from the group consisting of: linoleic acid, gamma-linolenic acid, eicosadienoic acid, dihomo-gamma-linolenic acid, arachidonic acid, docosadienoic acid, adrenic acid, docosapentaenoic acid, tetracosatetraenoic acid, tetracosapentaenoic acid, and combinations thereof.

26. The therapeutic nanoparticle of claim 22, wherein the fatty acid is an omega-9 fatty acid selected from the group consisting of: oleic acid, eicosenoic acid, mead acid, erucic acid, nervonic acid, and combinations thereof.

27. The therapeutic nanoparticle of claim 26, wherein the fatty acid is oleic acid.

28. The therapeutic nanoparticle of claim 27 wherein the weight ratio of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea to oleic acid is about 6:1.

29. The therapeutic nanoparticle of claim 22, wherein the fatty acid is a polyunsaturated fatty acid selected from the group consisting of: rumenic acid, α-calendic acid, β-calendic acid, jacaric acid, α-eleostearic acid, β-eleostearic acid, catalpic acid, punicic acid, rumelenic acid, α-parinaric acid, β-parinaric acid, bosseopentaenoic acid, pinolenic acid, podocarpic acid, and combinations thereof.

30. The therapeutic nanoparticle of any one of claims 1-22, wherein the hydrophobic

acid is a bile acid.

31. The therapeutic nanoparticle of claim 30, wherein the bile acid is selected from the group consisting of chenodeoxycholic acid, ursodeoxycholic acid, deoxycholic acid, hycholic acid, beta-muricholic acid, cholic acid, lithocholic acid, an amino acid-conjugated bile acid, and combinations thereof.

32. The therapeutic nanoparticle of claim 31, wherein the bile acid is cholic acid.

33. The therapeutic nanoparticle of claim 31, wherein the amino acid-conjugated bile acid is a glycine-conjugated bile acid or a taurine-conjugated bile acid.

34. The therapeutic nanoparticle of any one of claims 1-21, wherein the hydrophobic acid is selected from the group consisting of dioctyl sulfosuccinic acid, 1-hydroxy-2-naphthoic acid, dodecylsulfuric acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, pamoic acid, undecanoic acid, and combinations thereof.

35. The therapeutic nanoparticle of claim 34, wherein the hydrophobic acid is pamoic acid.

36. The therapeutic nanoparticle of claim 35 wherein the weight ratio of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea to pamoic acid is about 1.8:1.

37. The therapeutic nanoparticle of any one of claims 1-36, comprising about 1 to about 20 weight percent of the therapeutic agent.

38. The therapeutic nanoparticle of any one of claims 1-36, comprising about 2 to about 20 weight percent of the therapeutic agent.

39. The therapeutic nanoparticle of any one of claims 1-36, comprising about 4 to about 20 weight percent of the therapeutic agent.

40. The therapeutic nanoparticle of any one of claims 1-36, comprising about 5 to about 20 weight percent of the therapeutic agent.

41. The therapeutic nanoparticle of any one of claims 1-36, wherein the hydrophobic acid has a molecular weight of between about 200 Da and about 800 Da.

42. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle substantially retains the therapeutic agent for at least 1 minute when placed in a phosphate buffer solution at 37 °C.

43. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle substantially immediately releases less than about 30% of the therapeutic agent when placed in a phosphate buffer solution at 37 °C.

44. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 10 to about 45% of the therapeutic agent over about 1 hour when placed in a phosphate buffer solution at 37 °C.

45. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 4 hours when placed in a phosphate buffer solution at 37 °C.

46. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 10 hours when placed in a phosphate buffer solution at 37 °C.

47. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 0.01 to about 25% of the therapeutic agent over about 20 hours when placed in a phosphate buffer solution at 37 °C.

48. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle releases about 1 to about 40% of the therapeutic agent over about 40 hours when placed in a phosphate buffer solution at 37 °C.

49. The therapeutic nanoparticle of any one of claims 1-41, wherein the therapeutic nanoparticle has a release profile that is substantially the same as a release profile for a control nanoparticle that is substantially the same as the therapeutic nanoparticle except that it does not contain a fatty acid or bile acid.

50. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.6 to about 0.95.

51. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.6 to about 0.8.

52. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.75 to about 0.85.

53. The therapeutic nanoparticle of any one of claims 1-49, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a poly(lactic) acid number average molecular weight fraction of about 0.7 to about 0.9.

54. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 10 to about 25 weight percent poly(ethylene)glycol.

55. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 10 to about 20 weight percent poly(ethylene)glycol.

56. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 15 to about 25 weight percent poly(ethylene)glycol.

57. The therapeutic nanoparticle of any one of claims 1-53, wherein the therapeutic nanoparticle comprises about 20 to about 30 weight percent poly(ethylene)glycol.

58. The therapeutic nanoparticle of any one of claims 1-57, wherein the poly(lactic) acid-poly(ethylene)glycol copolymer has a number average molecular weight of about 15 kDa to about 20 kDa poly(lactic acid) and a number average molecular weight of about 4 kDa to about 6 kDa poly(ethylene)glycol.

59. The therapeutic nanoparticle of any one of claims 1-58, further comprising about 0.2 to about 30 weight percent poly(lactic) acid-poly(ethylene)glycol copolymer functionalized

with a targeting ligand.

60. The therapeutic nanoparticle of any one of claims 1-58, further comprising about 0.2 to about 30 weight percent poly(lactic) acid-co-poly(glycolic) acid-poly(ethylene)glycol copolymer functionalized with a targeting ligand.

61. The therapeutic nanoparticle of claim 59 or 60, wherein the targeting ligand is covalently bound to the poly(ethylene)glycol.

62. The therapeutic nanoparticle of any one of claims 1-61, wherein the hydrophobic acid is a polyelectrolyte.

63. The therapeutic nanoparticle of claim 62, wherein the polyelectrolyte is selected from the group consisting of a poly(styrene sulfonic acid), polypolyacrylic acid, and polymethacrylic acid.

64. The therapeutic nanoparticle of any one of claims 1-63, wherein the substantially hydrophobic acid is a mixture of two or more substantially hydrophobic acids.

65. The therapeutic nanoparticle of claim 64, comprising a mixture of two substantially hydrophobic acids.

66. The therapeutic nanoparticle of claim 65, wherein the two substantially hydrophobic acids are oleic acid and cholic acid.

67. The therapeutic nanoparticle of claim 64, comprising a mixture of three substantially hydrophobic acids.

68. The therapeutic nanoparticle of claim 64, comprising a mixture of four substantially hydrophobic acids.

69. The therapeutic nanoparticle of claim 64, comprising a mixture of five substantially hydrophobic acids.

70. A therapeutic nanoparticle prepared by the process comprising the steps of: emulsification of a first organic phase comprising a first polymer, a therapeutic

agent, and a substantially hydrophobic acid, thereby forming an emulsion phase;

quenching of the emulsion phase thereby forming a quenched phase; and

filtration of the quenched phase to recover the therapeutic nanoparticles, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

71. The therapeutic nanoparticle of claim 70, wherein the hydrophobic acid is a fatty acid.

72. The therapeutic nanoparticle of claim 71, wherein the fatty acid is a saturated fatty acid selected from the group consisting of: caproic acid, enanthic acid, caprylic acid, pelargonic acid, capric acid, undecanoic acid, lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, nonadecylic acid, arachidic acid, heneicosylic acid, behenic acid, tricosylic acid, lignoceric acid, pentacosylic acid, cerotic acid, heptacosylic acid, montanic acid, nonacosylic acid, melissic acid, henatriacontylic acid, lacceroic acid, psyllic acid, geddic acid, ceroplastic acid, hexatriacontylic acid, and combinations thereof.

73. The therapeutic nanoparticle of claim 71, wherein the fatty acid is an omega-3 fatty acid selected from the group consisting of: hexadecatrienoic acid, alpha-linolenic acid, stearidonic acid, eicosatrienoic acid, eicosatetraenoic acid, eicosapentaenoic acid, heneicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid, tetracosapentaenoic acid, tetracosahexaenoic acid, and combinations thereof.

74. The therapeutic nanoparticle of claim 71, wherein the fatty acid is an omega-6 fatty acid selected from the group consisting of: linoleic acid, gamma-linolenic acid, eicosadienoic acid, dihomo-gamma-linolenic acid, arachidonic acid, docosadienoic acid, adrenic acid, docosapentaenoic acid, tetracosatetraenoic acid, tetracosapentaenoic acid, and combinations thereof.

75. The therapeutic nanoparticle of claim 71, wherein the fatty acid is an omega-9 fatty acid selected from the group consisting of: oleic acid, eicosenoic acid, mead acid, erucic

acid, nervonic acid, and combinations thereof.

76. The therapeutic nanoparticle of claim 75, wherein the fatty acid is oleic acid.

77. The therapeutic nanoparticle of claim 71, wherein the fatty acid is a polyunsaturated fatty acid selected from the group consisting of: rumenic acid, α-calendic acid, β-calendic acid, jacaric acid, α-eleostearic acid, β-eleostearic acid, catalpic acid, punicic acid, rumelenic acid, α-parinaric acid, β-parinaric acid, bosseopentaenoic acid, pinolenic acid, podocarpic acid, and combinations thereof.

78. The therapeutic nanoparticle of claim 70, wherein the hydrophobic acid is a bile acid.

79. The therapeutic nanoparticle of claim 78, wherein the bile acid is selected from the group consisting of chenodeoxycholic acid, ursodeoxycholic acid, deoxycholic acid, hycholic acid, beta-muricholic acid, cholic acid, lithocholic acid, an amino acid-conjugated bile acid, and combinations thereof.

80. The therapeutic nanoparticle of claim 79, wherein the bile acid is cholic acid.

81. The therapeutic nanoparticle of claim 79, wherein the amino acid-conjugated bile acid is a glycine-conjugated bile acid or a taurine-conjugated bile acid.

82. The therapeutic nanoparticle of claim 70, wherein the hydrophobic acid is selected from the group consisting of dioctyl sulfosuccinic acid, 1-hydroxy-2-naphthoic acid, dodecylsulfuric acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, pamoic acid, undecanoic acid, and combinations thereof.

83. The therapeutic nanoparticle of claim 82, wherein the hydrophobic acid is pamoic acid.

84. The therapeutic nanoparticle of any one of claims 70-83, wherein the hydrophobic acid has a molecular weight of between about 200 Da and about 800 Da.

85. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle substantially retains the therapeutic agent for at least 1 minute when placed in a

phosphate buffer solution at 37 °C.

86. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle substantially immediately releases less than about 30% of the therapeutic agent when placed in a phosphate buffer solution at 37 °C.

87. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 10 to about 45% of the therapeutic agent over about 1 hour when placed in a phosphate buffer solution at 37 °C.

88. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 4 hours when placed in a phosphate buffer solution at 37 °C.

89. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 0.01 to about 15% of the therapeutic agent over about 10 hours when placed in a phosphate buffer solution at 37 °C.

90. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 0.01 to about 25% of the therapeutic agent over about 20 hours when placed in a phosphate buffer solution at 37 °C.

91. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle releases about 1 to about 40% of the therapeutic agent over about 40 hours when placed in a phosphate buffer solution at 37 °C.

92. The therapeutic nanoparticle of any one of claims 70-84, wherein the therapeutic nanoparticle has a release profile that is substantially the same as a release profile for a control nanoparticle that is substantially the same as the therapeutic nanoparticle except that it does not contain a fatty acid or bile acid.

93. The therapeutic nanoparticle of any one of claims 70-92, wherein the first polymer is poly(lactic) acid-poly(ethylene)glycol copolymer.

94. The therapeutic nanoparticle of any one of claims 70-92, wherein the first polymer is

poly(lactic) acid-co-poly(glycolic) acid-poly(ethylene)glycol copolymer.

95. The therapeutic nanoparticle of any one of claims 70-94, wherein the substantially hydrophobic acid is a mixture of two or more substantially hydrophobic acids.

96. The therapeutic nanoparticle of claim 95, comprising a mixture of two substantially hydrophobic acids.

97. The therapeutic nanoparticle of claim 95, comprising a mixture of three substantially hydrophobic acids.

98. The therapeutic nanoparticle of claim 95, comprising a mixture of four substantially hydrophobic acids.

99. The therapeutic nanoparticle of claim 95, comprising a mixture of five substantially hydrophobic acids.

100. The therapeutic nanoparticle of any one of claims 1, 5-93, or 95-99 wherein the polymer is PLA-PEG and the mole ratio of PLA-PEG is 5:1.

101. A therapeutic nanoparticle prepared by the process comprising the steps of:

combining a first organic phase with a first aqueous solution to form a second phase;

emulsifying the second phase to form an emulsion phase, wherein the emulsion phase comprises a first polymer, therapeutic agent, and a substantially hydrophobic acid;

quenching of the emulsion phase thereby forming a quenched phase; and

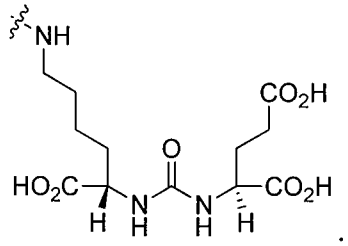
filtering the quenched phase to recover the therapeutic nanoparticles, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea, the first organic phase comprises the therapeutic agent and pamoic acid in a weight ratio of therapeutic agent to pamoic acid of about 11:1 and PLA-PEG (in a 16:5 molar ratio) in a weight ratio of therapeutic agent to PLA-PEG of about 1:3 in an organic solvent comprising of benzyl alcohol and ethyl acetate in a weight ratio of benzyl alcohol to ethyl acetate of about 1.25 and the first aqueous solution comprises a polyoxyethylene (100) stearyl ether dissolved in benzyl alcohol in a weight ratio of 0.005:1 and combining the first organic phase and the first aqueous phase in

a weight ratio of about 1:5 to form a second phase and emulsifying the second phase formed therefrom and quenching the emulsion phase with 0.1 M citric acid in water solution at pH 4.5 and concentrating the resulting product.

102. A therapeutic nanoparticle of 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or pharmaceutically acceptable salt thereof.

103. A therapeutic nanoparticle comprising of a therapeutic agent or a pharmaceutically acceptable salt thereof and a polymer selected from diblock poly(lactic) acid-poly(ethylene)glycol copolymer or a diblock poly(lactic acid-co-glycolic acid)-poly(ethylene)glycol copolymer and combinations thereof, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

104. The therapeutic nanoparticle of any one of claims 1-69, 102, or 103, wherein a targeting ligand is additionally present and is PLA-PEG-GL, wherein GL has the following structure:



105. The therapeutic nanoparticle according to any one of claims 1-69 or 102-104, further comprising a solubilizer.

106. The therapeutic nanoparticle according to claim 105, wherein the solubilizer is polysorbate 80.

107. The therapeutic nanoparticle of claim 105, wherein the solubilizer is polyoxyethylene (100) stearyl ether.

108. The therapeutic nanoparticle of any one of claims 1-107, wherein the therapeutic

agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea.

109. A pharmaceutical composition comprising a therapeutic nanoparticle of any one of claims 1-108 and a pharmaceutically acceptable excipient.

110. The pharmaceutical composition of claim 109 comprising a plurality of therapeutic nanoparticles.

111. The pharmaceutical composition of claim 109 or 110, further comprising a saccharide.

112. The pharmaceutical composition of any one of claims 109-111, further comprising a cyclodextrin.

113. The pharmaceutical composition of claim 111 or 112, wherein the saccharide is a disaccharide selected from the group consisting of sucrose, trehalose, and a mixture thereof.

114. Use of a therapeutically effective amount of a therapeutic nanoparticle of any one of claims 1-108 or a pharmaceutical composition of any one of claims 109-113 in the manufacture of a medicament for treating cancer in a subject in need thereof.

115. The use of claim 114, wherein the cancer is chronic myelogenous leukemia.

116. The use of claim 114, wherein the cancer is gastrointestinal stromal tumor.

117. The use of claim 114, wherein the cancer is selected from the group consisting of chronic myelomonocytic leukemia, hypereosinophilic syndrome, renal cell carcinoma, hepatocellular carcinoma, Philadelphia chromosome positive acute lymphoblastic leukemia, non-small cell lung cancer, pancreatic cancer, breast cancer, a solid tumor, head and neck cancer and mantle cell lymphoma.

118. The use of claim 117, wherein the cancer is breast cancer.

119. A process for preparing a therapeutic nanoparticle, comprising the steps of:
combining a first organic phase with a first aqueous solution to form a second phase;

emulsifying the second phase to form an emulsion phase, wherein the emulsion phase comprises a first polymer, therapeutic agent, and a substantially hydrophobic acid;

quenching of the emulsion phase thereby forming a quenched phase; and

filtering the quenched phase to recover the therapeutic nanoparticles, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea or a pharmaceutically acceptable salt thereof.

120. The process of claim 119, further comprising combining the therapeutic agent and the substantially hydrophobic acid in the second phase prior to emulsifying the second phase.

121. The process of claim 120, wherein the therapeutic agent and the substantially hydrophobic acid form a hydrophobic ion pair prior to emulsifying the second phase.

122. The process of claim 120, wherein the therapeutic agent and the substantially hydrophobic acid form a hydrophobic ion pair prior during emulsification of the second phase.

123. The process of claim 119, further comprising combining the therapeutic agent and the substantially hydrophobic acid in the second phase substantially concurrently with emulsifying the second phase.

124. The process of claim 119, wherein the first organic phase comprises the therapeutic agent and the first aqueous solution comprises the substantially hydrophobic acid.

125. The process of any one of claims 119-124, wherein the therapeutic agent, when protonated, has a first pK_a, the substantially hydrophobic acid has a second pK_a, and the emulsion phase is quenched with an aqueous solution having a pH equal to a pK_a unit between the first pK_a and the second pK_a.

126. The process of claim 125, wherein the quenched phase has a pH equal to a pK_a unit between the first pK_a and the second pK_a.

127. The process of any one of claims 119-126, wherein the therapeutic agent, when

protonated, has a first pK_a, the substantially hydrophobic acid has a second pK_a, and the first aqueous solution has a pH equal to a pK_a unit between the first pK_a and the second pK_a.

128. The process of any one of claims 125-127, wherein the pH is equal to a pK_a unit that is about equidistant between the first pK_a and the second pK_a.

129. The process of any one of claims 119-128, wherein the therapeutic agent is 1-(4-{[4-(dimethylamino)piperidin-1-yl]carbonyl}phenyl)-3-[4-(4,6-dimorpholin-4-yl-1,3,5-triazin-2-yl)phenyl]urea.