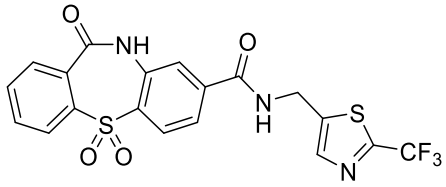
What is claimed:

1. A pharmaceutical composition comprising:

a solid dispersion, wherein the solid dispersion comprises:

a compound represented by:



or a pharmaceutically acceptable salt thereof, and

a polymer;

wherein the solid dispersion comprises about 10 wt % to about 50 wt % of the compound, or a pharmaceutically acceptable salt thereof, and about 40 wt % to about 90 wt % of the polymer.

2. The pharmaceutical composition of claim 1, wherein the solid dispersion comprises about 15 wt % to about 30 wt % of compound, or a pharmaceutically acceptable salt thereof, and about 70 wt % to about 90 wt % of the polymer.

3. The pharmaceutical composition of claim 1 or 2, wherein the polymer is a methacrylate polymer or a cellulosic polymer.

4. The pharmaceutical composition of any one of claims 1-3, wherein the polymer is selected from the group consisting of poly(methacrylic acid-co-methyl methacrylate), hypromellose acetate succinate, and hydroxypropyl methylcellulose phthalate.

5. The pharmaceutical composition of any one of claims 1-4, wherein the solid dispersion is a spray-dried solid dispersion.

6. The pharmaceutical composition of any one of claims 1-5, wherein the solid dispersion is a substantially amorphous solid dispersion.

7. The pharmaceutical composition of any one of claims 1-5, wherein the solid dispersion is an amorphous solid dispersion.

8. The pharmaceutical composition of claim 6 or 7, wherein the solid dispersion has a single T_g.

9. The pharmaceutical composition of claim 8, wherein the solid dispersion is stable for at least four weeks.

10. The pharmaceutical composition of any one of claims 1-9, wherein the pharmaceutical composition further comprises an excipient.

11. The pharmaceutical composition of claims 10, wherein the solid dispersion further comprises an excipient.

12. The pharmaceutical composition of claim 10 or 11, wherein the excipient is selected from the group consisting of a filler, a sweetener, diluent, binder, lubricant, disintegrant, and glidant.

13. The pharmaceutical composition of claim 10 or 11, wherein the excipient is selected from the group consisting of microcrystalline cellulose, mannitol, talc, croscarmellose sodium, magnesium stearate, and sodium lauryl sulfate.

14. The pharmaceutical composition of claim 10 or 11, wherein the pharmaceutical composition further comprises a colorant, a fragrance, or flavoring agent.

15. The pharmaceutical composition of any one of claims 1-14, wherein the pharmaceutical composition is in a dose form selected from the group consisting of a granule, a pellet, a tablet, a particle, and a mini-tablet.

16. The pharmaceutical composition of any one of claims 1-15, wherein the pharmaceutical composition comprises a pharmaceutically effective amount of the compound or a pharmaceutically acceptable salt thereof.

17. The pharmaceutical composition of any one of claims 1-16, wherein the pharmaceutical composition is in a dose form comprising about 75 mg to about 125 mg of the compound, or a pharmaceutically acceptable salt thereof.

18. Use of a pharmaceutical composition according to any one of claims 1-17 in the manufacture of a medicament for treating Hepatitis B (HBV) in a patient in need thereof, wherein a therapeutically effective amount of the pharmaceutical composition is to be administered to the patient.

19. A method for preparing a pharmaceutical composition, the method comprising:

combining 11-oxo-N-((2-(trifluoromethyl)thiazol-5-yl)methyl)-10,11-dihydrodibenzo[b,f][1,4]thiazepine-8-carboxamide 5,5-dioxide, or a pharmaceutically acceptable salt thereof, and a polymer in a solvent thereby forming a mixture,

drying the mixture thereby forming a solid dispersion; and

optionally combining the solid dispersion with an excipient.

20. The method of claim 19, wherein drying the mixture comprises spray drying the mixture.

21. The method of claim 19 or 20, wherein the solvent comprises water.

22. The method of any one of claims 19-21, wherein the solvent comprises an organic solvent.

23. The method of any one of claims 19-22, wherein the solvent comprises acetone and water.

24. The method of any one of claims 19-23, wherein the polymer is selected from the group consisting of poly(methacrylic acid-co-methyl methacrylate), hypromellose acetate succinate, and hydroxypropyl methylcellulose phthalate.

25. The method of any one of claims 19-24, wherein the solid dispersion is a substantially amorphous solid dispersion ion.

26. The method of any one of claims 19-24, wherein the solid dispersion is an amorphous solid dispersion.

27. The method of claim 25 or 26, wherein the solid dispersion has a single T_g.

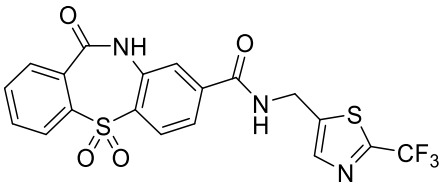
28. The method of any one of claims 19-27, wherein the excipient is selected from the group consisting of a filler, sweetener, diluent, binder, lubricant, disintegrant, and glidant.

29. The method of any one of claims 18-26, wherein the excipient is selected from the group consisting of microcrystalline cellulose, mannitol, talc, croscarmellose sodium, magnesium stearate, and sodium lauryl sulfate.

30. The method of any one of claims 19-29, wherein the solid dispersion comprises about 10 wt % to about 50 wt % of 11-oxo-N-((2-(trifluoromethyl)thiazol-5-yl)methyl)-10,11-dihydrodibenzo[b,f][1,4]thiazepine-8-carboxamide 5,5-dioxide, or a pharmaceutically acceptable salt thereof, and about 40 wt % to about 90 wt % of the polymer.

31. The method of any one of claims 19-29, wherein the solid dispersion comprises about 15 wt % to about 30 wt % of 11-oxo-N-((2-(trifluoromethyl)thiazol-5-yl)methyl)-10,11-dihydrodibenzo[b,f][1,4]thiazepine-8-carboxamide 5,5-dioxide, or a pharmaceutically acceptable salt thereof, and about 70 wt % to about 90 wt % of the polymer.

32. The method of any one of claims 19-31, further comprising: compressing the pharmaceutical composition into a tablet.

33. Use of a compound represented by:  in the manufacture of a medicament for treating hepatitis B in a subject in need thereof, wherein:

about 300 mg of the compound is to be administered daily to the subject

and wherein a therapeutically effective amount of a nucleos(t)ide inhibitor selected from the group consisting of entecavir, tenofovir and tenofovir alafenamide fumarate is to be administered to the subject.

34. The use of claim 33, wherein the subject is virologically suppressed and HBeAg negative before the compound is to be administered.

35. The use of claim 33, wherein the subject is virologically suppressed and HBeAg positive before the compound is to be administered.

36. The use of claim 33, wherein the subject is treatment naïve and HBeAg positive before the compound is to be administered.

37. The use of claim 33, wherein the subject is virologically suppressed for at least 6 months before administration of the compound and has previously been administered a nucleos(t)ide inhibitor alone.

38. The use of claim 33 or 34, wherein the subject has been previously administered a nucleos(t))ide inhibitor alone for at least 2 months before administration of the compound.

39. The use of claim 33, wherein the subject has not been previously administered nucleos(t)ide inhibitor before administration of the compound.

40. The use of any one of claims 33-36, wherein the subject has detectable levels of hepatitis B viral DNA prior to administration.

38. The use of any one of claims 33-36, wherein the subject is HBeAg positive before administration of the compound.

39. The use of claim 37, wherein after 24 weeks of daily administration, the HBeAg positive subject has sustained HBeAg loss of <0.11 PEI units/mL.

40. The use of claim 37, wherein after 12 weeks of daily administration, the HBeAg positive subject has sustained HBeAg loss of <0.11 PEI units/mL.

41. The use of claim 37, wherein after 28 weeks of daily administration, the HBeAg positive subject has sustained HBeAg loss of <0.11 PEI units/mL.

42. The use of claim 37, wherein after 32 weeks of daily administration, the HBeAg positive subject has sustained HBeAg loss of <0.11 PEI units/mL.

43. The use of claim 37, wherein after 36 weeks of daily administration, the HBeAg positive subject has sustained HBeAg loss of <0.11 PEI units/mL.

44. The use of claim 37, wherein after 42 weeks of daily administration, the HBeAg positive subject has sustained HBeAg loss of <0.11 PEI units/mL.

45. The use of claim 37, wherein after 44 weeks of daily administration, the HBeAg positive subject has sustained HBeAg loss of <0.11 PEI units/mL.

46. The use of any one of claims 33-37, wherein the subject is HBeAg negative before administration of the compound.

47. The use of any one of claims 33-46, wherein the compound is to be administered daily for at least 12 weeks, 24 weeks, 28 weeks, 32 weeks, 40 weeks, 44 weeks, 12 months, 18 months, 24 months, or 36 months.

48. The use of any one of claims 33- 47, wherein after 12 weeks, 24 weeks, 28 weeks, 32 weeks, 40 weeks, 44 weeks, 12 months, 18 months, 24 months, or 36 months of daily administration the subject has a reduction of HBeAg and/or HBsAg.

49. The use of claim 33-43, wherein after 12 weeks, 24 weeks, 28 weeks, 32 weeks, 40 weeks, 44 weeks, 12 months, 18 months, 24 months, or 36 months of daily administration the subject has a loss or stable reduction of HBsAg to ≤ 100 IU/mL.

50. The use of any one of claims 33-49, wherein after 12 weeks, 24 weeks, 28 weeks, 32 weeks, 40 weeks, 44 weeks, 12 months, 18 months, 24 months, or 36 months of daily administration the subject has sustained viral suppression.

51. The use of claim 33, wherein after 12 weeks, 24 weeks, 28 weeks, 32 weeks, 40 weeks, 44 weeks, 12 months, 18 months, 24 months, or 36 months of daily administration the subject has a reduction in HBV DNA or HBV RNA.

52. The use of claim 51, wherein the HBV DNA reduction is below the detectable limit using a PCR-assay.

53. The use of claim 51 or 52, wherein the HBV RNA is below the limit of detection.

54. The use of any one of claims 1-21, after 12 weeks, 24 weeks, 28 weeks, 32 weeks, 40 weeks, 44 weeks, 12 months, 18 months, 24 months, or 36 months of daily administration the subject has greater than $0.5\log_{10}$ decline in HBeAg.

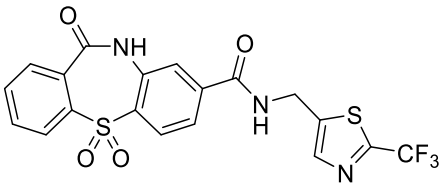
55. The use of any one of claims 33-54, for reducing hepatitis B virus to below detection levels in the subject.

56. The use of any one of claims 33-55, wherein the compound is in a solid dosage form.

57. The use of any one of claims 33-55, wherein the compound is in a solid dispersion.

58. The use of any one of claim 33-57 wherein the solid dispersion further comprises a polymer.

59. The use of any one of claim 33-57 wherein the solid dispersion further comprises an excipient.

60. Use of a compound represented by:  in the manufacture of a medicament for treating hepatitis B in a subject who is virologically suppressed and HBeAg negative, wherein:

about 300 mg of the compound is to be administered daily to the subject

and

wherein a therapeutically effective amount of a nucleos(t)ide inhibitor selected from the group consisting of entecavir, tenofovir and tenofovir alafenamide fumarate is to be administered to the subject;

wherein the subject was virologically suppressed and HBeAg negative before administration of the compound; and

wherein if after the 76th week of administering the compound and the nucleos(t)ide the subject has a hepatitis B viral DNA concentration of less than 20 IU/mL and a HBeAg concentration of less than or equal to 5 IU/mL for at least six months prior to the 76th week of administering the compound, administration of the compound and the nucleos(t)ide inhibitor is to be stopped.

61. The use of claim 60, wherein the subject is to be monitored for up to three years for hepatitis B viral DNA concentration and HBeAg concentration after the 76th week of administering the compound.

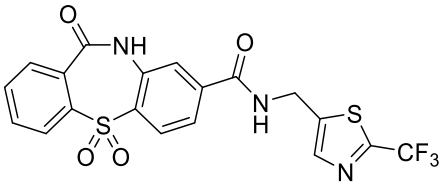
63. The use of claim 60, wherein the nucleos(t)ide inhibitor is entecavir.

64. The use of claim 60, wherein the compound is in a solid dosage form.

65. The use of claim 60, wherein the compound is in a solid dispersion.

66. The use of claim 65, wherein the solid dispersion further comprises a polymer.

67. The use of claim 65, wherein the solid dispersion further comprises an excipient.

68. Use of a compound represented by:  in the manufacture of a medicament for treating hepatitis B in a subject who is virologically suppressed and HBeAg positive, wherein :

about 300 mg of the compound is to be administered daily

and

wherein a therapeutically effective amount of a nucleos(t)ide inhibitor selected from the group consisting of entecavir, tenofovir and tenofovir alafenamide fumarate is to be administered to the subject;

wherein the subject was virologically suppressed and HBeAg positive before administration of the compound;

wherein if, after 76 weeks of administering the compound and the nucleosi(t)e the subject has a hepatitis B viral DNA concentration of less than 20 IU/mL and a HBeAg concentration of less than or equal to 5 IU/mL for at least six months prior to the 76th week, the administration of the compound and the nucleos(t)ide inhibitor is to be stopped; or

after 76 weeks of administering the compound, the subject has a hepatitis B viral DNA concentration of greater than or equal to 20 IU/mL or a HBeAg concentration of greater than 5 IU/mL during the six months prior to the 76th week of administering the compound, administration of the compound is stopped and administration of the nucleos(t)ide inhibitor is to be continued.

69. The use of claim 68, wherein the subject is to be monitored for up to three years after the 76th week of administering the compound for hepatitis B viral DNA concentration and HBeAg concentration if the subject has a hepatitis B viral DNA concentration of less than 20 IU/mL and a HBeAg concentration of less than or equal to 5 IU/mL for at least six months prior to the 76th week of administering the compound.

70. The use of claim 68, wherein the subject is to be monitored for up to twelve weeks after the 76th week of administering the compound for hepatitis B viral DNA concentration and HBeAg concentration if the subject has a hepatitis B viral DNA concentration of greater than or equal to 20 IU/mL or a HBeAg concentration of greater than 5 IU/mL during the six months prior to the 76th week of administering the compound.

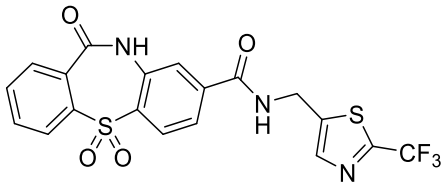
71. The use of claim 68, wherein the nucleos(t)ide inhibitor is entecavir.

72. The use of claim 68, wherein the compound is a solid dosage form.

73. The use of claim 68, wherein the compound is in a solid dispersion.

74. The use of claim 73, wherein the solid dispersion further comprises a polymer.

75. The use of claim 73, wherein the solid dispersion further comprises an excipient.

76. Use of a compound represented by:  in the manufacture of a medicament for treating hepatitis B in subject who is treatment naïve and HBeAg positive, wherein:

about 300 mg of the compound is to be administered daily to the subject and

wherein a therapeutically effective amount of a nucleos(t)ide inhibitor selected from the group consisting of entecavir, tenofovir and tenofovir alafenamide fumarate is to be administered to the subject;

wherein the subject was treatment naive and HBeAg positive before administration of the compound; and

wherein if after 76 weeks of administering the compound and the nucleosi(t)e the subject has a pgRNA decline of greater than or equal to 2.5 $\log_{10}$ U/mL from baseline for at least six months prior to the 76th week of administering the compound, administration of the compound and nucleos(t)ide inhibitor is to be continued up to 48 weeks; or

after 76 weeks of administering the compound and the nucleosi(t)e the subject has a pgRNA decline of less than 2.5 $\log_{10}$ U/mL from baseline during the six months prior to the 76th week of administering the compound, administration of the compound is to be stopped and administration of the nucleos(t)ide inhibitor is to be continued.

78. The use of claim 68, wherein the subject is to be monitored for up to twelve weeks after the 76th week of administering the compound for hepatitis B viral DNA concentration and HBeAg concentration if the subject has a pgRNA decline of less than 2.5 $\log_{10}$ U/mL from baseline during the six months prior to the 76th week of administering the compound.

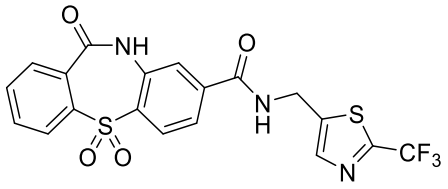
79. The use of claim 68, wherein the nucleos(t)ide inhibitor is entecavir.

80. The use of claim 68, wherein the compound is in a solid dosage form.

81. The use of claim 68, wherein the compound is in a solid dispersion.

82. The use of claim 81, wherein the solid dispersion further comprises a polymer.

83. The use of claim 81, wherein the solid dispersion further comprises an excipient.

84. Use of a compound represented by:  in the manufacture of a medicament for treating hepatitis B in subject who is treatment naïve and HBeAg positive, wherein:

about 300 mg of the compound is to be administered daily to the subject

and

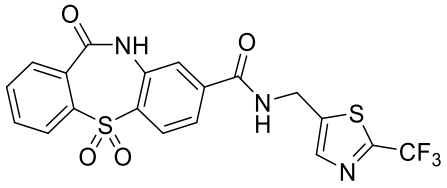
wherein a therapeutically effective amount of a nucleos(t)ide inhibitor selected from the group consisting of entecavir, tenofovir and tenofovir alafenamide fumarate is to be administered to the subject;

wherein the subject was treatment naive and HBeAg positive before administration of the compound; and

wherein if after 76 weeks of administering the compound and the nucleosi(t)e the subject has a pgRNA decline of greater than or equal to 2.5 $\log_{10}$ U/mL from baseline, administration of the compound and nucleos(t)ide inhibitor is to be continued up to 48 weeks; or

after 76 weeks of administering the compound and the nucleosi(t)e the subject has a pgRNA decline of less than 2.5 $\log_{10}$ U/mL from baseline, administration of the compound is stopped and administration of the nucleos(t)ide inhibitor is to be continued.

85. The use of claim 84, wherein the subject is to be monitored for up to twelve weeks after the 76th week of administering the compound for hepatitis B viral DNA concentration and HBeAg concentration if the subject has a pgRNA decline of less than 2.5 $\log_{10}$ U/mL from baseline.

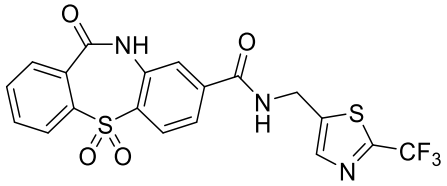
86. Use of a compound represented by:  in the manufacture of a medicament for treating hepatitis B in a subject who is to be virologically suppressed and HBeAg negative, wherein:

about 300 mg of the compound is to be administered daily to the subject and

wherein a therapeutically effective amount of a nucleos(t)ide inhibitor selected from the group consisting of entecavir, tenofovir and tenofovir alafenamide fumarate is to be administered to the subject;

wherein the subject was virologically suppressed and HBeAg negative before administration of the compound; and

wherein if after the 52nd week of administering the compound and the nucleos(t)ide the subject has a hepatitis B viral DNA concentration of less than 20 IU/mL and a HBeAg concentration of less than or equal to 5 IU/mL for at least six months prior to the 52nd week of administering the compound, administration of the compound and the nucleos(t)ide inhibitor is to be stopped.

87. Use of a compound represented by:  in the manufacture of a medicament for treating hepatitis B in a subject who is to be virologically suppressed and HBeAg positive, wherein:

about 300 mg of the compound is to be administered daily to the subject and

wherein a therapeutically effective amount of a nucleos(t)ide inhibitor selected from the group consisting of entecavir, tenofovir and tenofovir alafenamide fumarate is to be administered to the subject;

wherein the subject was virologically suppressed and HBeAg positive before administration of the compound;

wherein if, after 52 weeks of administering the compound and the nucleosi(t)e the subject has a hepatitis B viral DNA concentration of less than 20 IU/mL and a HBeAg

concentration of less than or equal to 5 IU/mL for at least six months prior to the 52nd week, the administration of the compound and the nucleos(t)ide inhibitor is to be stopped; or

after 52 weeks of administering the compound, the subject has a hepatitis B viral DNA concentration of greater than or equal to 20 IU/mL or a HBeAg concentration of greater than 5 IU/mL during the six months prior to the 52nd week of administering the compound, administration of the compound is to be stopped and administration of the nucleos(t)ide inhibitor is to be continued.