WHAT IS CLAIMED:

1. A formulation comprising: (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in an amount of about 0.01 to about 0.15%, and hydroxypropyl β-cyclodextrin or sulfobutyl ether-beta-cyclodextrin in an amount of about 99.1 to about 99.99%, based on the total weight of the formulation.

2. The formulation of claim 1 comprising: (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in an amount of about 0.08 to about 0.15%, and hydroxypropyl β-cyclodextrin or sulfobutyl ether-beta-cyclodextrin in an amount of about 99.1 to about 99.9%, based on the total weight of the formulation.

3. The formulation of claim 1 or 2, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in the amount from about 0.1 to about 0.13% based on the total weight of the formulation.

4. The formulation of any one of claims 1-3, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in the amount of about 0.12% based on the total weight of the formulation.

5. The formulation of claim 1 comprising: (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in an amount of about 0.01 to about 0.08%, and hydroxypropyl β-cyclodextrin in an amount of about 99.40 to about 99.99%, based on the total weight of the formulation.

6. The formulation of claim 1 or 5, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate,

hydrate, co-crystal, clathrate, or polymorph thereof in the amount from about 0.03 to about 0.06% based on the total weight of the formulation.

7. The formulation of any one of claims 1 and 5-6, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof from about 0.1 to about 0.13%, hydroxypropyl β-cyclodextrin from about 99.1% to about 99.9%, and formic acid from about 0.05 to about 0.1% based on total weight of the formulation.

8. The formulation of any one of claims 1 and 5-7, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof from about 0.01 to about 0.08%, hydroxypropyl β-cyclodextrin from about 99.40% to about 99.99%, and formic acid from about 0.1 to about 0.3% based on total weight of the formulation.

9. The formulation of any one of claims 1-8 further comprising formic acid in an amount of no more than about 0.5%.

10. The formulation of any one of claims 1-9, comprising a solid form of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide).

11. The formulation of any one of claims 1-9, comprising an amorphous form of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide).

12. A formulation comprising: (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in an amount of about 0.08 to about 0.15%, a citrate buffer in an amount of about 3 to about 6%, and hydroxypropyl β-cyclodextrin or sulfobutyl ether-beta-cyclodextrin in an amount of about 94 to about 96% based on the total weight of the formulation.

13. The formulation of claim 12 comprising a solid form of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide).

14. The formulation of claim 12 comprising an amorphous form of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide).

15. The formulation of any one of claims 12-14, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in the amount from about 0.1 to about 0.13% based on the total weight of the formulation.

16. The formulation of any one of claims 12-15, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in the amount of about 0.12% based on the total weight of the formulation.

17. The formulation of any one of claims 12-16, comprising citrate buffer in the amount from about 3% to about 6% based on total weight of the formulation.

18. The formulation of any one of claims 12-17, wherein citrate buffer comprises anhydrous citric acid and anhydrous sodium citrate.

19. The formulation of claim 18, comprising anhydrous citric acid in the amount from about 2% to about 2.5% based on total weight of the formulation.

20. The formulation of claim 18, comprising anhydrous citric acid in the amount of about 2.1% based on total weight of the formulation.

21. The formulation of claim 18, comprising anhydrous sodium citrate in the amount from about 2% to about 2.5% based on total weight of the formulation.

22. The formulation of claim 21, comprising anhydrous sodium citrate in the amount of about 2.08% based on total weight of the formulation.

23. The formulation of any one of claims 12-22, comprising hydroxypropyl β-cyclodextrin in the amount from about 94% to about 97% based on total weight of the formulation.

24. The formulation of any one of claims 12-23, comprising hydroxypropyl β-cyclodextrin in the amount of about 95% based on total weight of the formulation.

25. The formulation of any one of claims 12-24 further comprising dimethyl sulfoxide in an amount of no more than about 1.5%.

26. The formulation of any one of claims 12-25, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a

stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof from about 0.1 to about 0.13%, anhydrous citric acid from about 2% to about 2.5%, anhydrous sodium citrate from about 2% to about 2.5%, hydroxypropyl β-cyclodextrin from about 94% to about 96%, and dimethyl sulfoxide from about 0.4 to about 1.5% based on total weight of the formulation.

27. An aqueous formulation comprising the formulation of any one of claims 1-26 and a diluent.

28. The aqueous formulation of claim 27, wherein the diluent is water or ½ normal saline.

29. The aqueous formulation of claim 27, wherein the diluent is normal saline.

30. The aqueous formulation of any one of claims 27-29, comprising (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in an amount of about 0.1 to 0.3 mg/mL.

31. The aqueous formulation of any one of claims 27-30, wherein the aqueous solution has a pH in a range from about 3.0 to about 3.6.

32. The aqueous formulation of any one of claims 27-30, wherein the aqueous solution has a pH in a range from about 4.2 to about 4.4.

33. The aqueous formulation of any one of claims 27-32, wherein the aqueous solution has an osmolality of about 260-280 mOsm/kg.

34. The aqueous formulation of any one of claims 27-32, wherein the aqueous solution has an osmolality of about 310-380 mOsm/kg.

35. Use of the formulation of any one of claims 1-26 or use of the aqueous formulation of any one of claims 27-34 in the manufacture of a medicament for treating a cancer in a mammal,, wherein the medicament is to be administered to the mammal.

36. The use of claim 35, wherein the aqueous formulation of any one of claims 27-34 is to be administered intravenously.

37. The use of claim 35 or 36, wherein the cancer is leukemia.

38. The use of claim 37, wherein the leukemia is chronic lymphocytic leukemia, chronic myelocytic leukemia, acute lymphoblastic leukemia or acute myeloid leukemia.

39. The use of any one of claims 35-38, wherein the medicament is to be administered in combination with a therapeutically effective amount of another second active agent or a supportive care therapy to the mammal.

40. The use of claim 39, wherein the other second active agent is a therapeutic antibody that specifically binds to a cancer antigen, a hematopoietic growth factor, a cytokine, anti-cancer agent, an antibiotic, a cox-2 inhibitor, an immunomodulatory agent, an immunosuppressive agent, a corticosteroid or a pharmacologically active mutant or derivative thereof.

41. Use of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in the manufacture of a medicament for treating a leukemia in a mammal, wherein the the medicament is to be administered in combination with a second agent selected from a JAK inhibitor, a FLT3 inhibitor, an mTOR inhibitor, a spiceosome inhibitor, an ERK inhibitor, an LSD1 inhibitor, an SMG1 inhibitor, a BH3 mimetic, and a topoisomerase inhibitor to the mammal.

42. The use of claim 41, wherein the second agent is selected from pladienolide B, chloro-N,N-diethyl-5-((4-(2-(4-(3-methylureido)phenyl)pyridin-4-yl)pyrimidin-2-yl)amino)benzenesulfonamide (compound Ii), venetoclax, topotecan and everolimus.

43. The use of claim 41, wherein the second agent is a JAK inhibitor.

44. The use of claim 43, wherein the JAK inhibitor is selected from tofacitinib, momelotinib, filgotinib, decernotinib, barcitinib, ruxolitinib, fedratinib, NS-018 and pacritinib.

45. The use of claim 41, wherein the second agent is a FLT3 inhibitor.

46. The use of claim 45, wherein the FLT3 inhibitor is selected from quizartinib, sunitinib, midostaurin, pexidartinib, lestaurtinib, tandutinib, and crenolanib.

47. The use of claim 41, wherein the second agent is everolimus.

48. The use of any one of claims 41-47, wherein the leukemia is an acute myeloid leukemia.

49. The use of any one of claims 41-48, wherein the leukemia is relapsed, refractory or resistant.

50. Use of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in the manufacture of a medicament for treating a myeloproliferative

neoplasm in a mammal, wherein the medicament is to be administered in combination with a JAK inhibitor to the mammal.

51. The use of claim 50, wherein the JAK inhibitor is selected from tofacitinib, momelotinib, filgotinib, decernotinib, barcitinib, ruxolitinib, fedratinib, NS-018 and pacritinib.

52. Use of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in the manufacture of a medicament for treating a cancer selected from breast cancer, neuroendocrine tumor, and renal cell carcinoma in a mammal, wherein the medicament is to be administered in combination with a second agent selected from everolimus, temsirolimus, 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one and 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((trans)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one to the mammal.

53. The use of claim 52, wherein the second agent is everolimus.

54. The use of any one of claims 41-53, wherein the formulation of any one of claims 1-26, or the aqueous formulation of any one of claims 27-34 is to be administered to the mammal.

55. Use of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof in combination with an IDH2 inhibitor to the mammal in the manufacture of a medicament for treating a leukemia in a mammal, wherein the wherein the medicament is to be administered to the mammal, wherein the leukemia is characterized by the presence of a mutant allele of IDH2.

56. The use of claim 54, wherein the IDH2 inhibitor is enasidenib or 6-(6-(trifluoromethyl)pyridin-2-yl)-N^2-(2-(trifluoromethyl)pyridin-4-yl)-1,3,5-triazine-2,4-diamine.

57. The use of claim 55 or 56, wherein the leukemia is an acute myeloid leukemia characterized by the presence of a mutant allele of IDH2.

58. The use of any one of claims 55-57, wherein the leukemia is relapsed, refractory or resistant.

59. Use of a combination of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of

stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof and a second agent in the manufacture of a medicament for reducing a level of GSPT1 in a subject, the medicament is to be administered to the subject.

60. Use of a combination of (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof and a second agent in the manufacture of a medicament for reducing a level of Mcl-1 in a subject, the medicament is to be administered to the subject.

61. The use of claim 59 or 60, wherein the second agent is selected from a JAK inhibitor, FLT3 inhibitor, mTOR inhibitor, spliceosome inhibitor, BET inhibitor, SMG1 inhibitor, ERK inhibitor, LSD1 inhibitor, BH3 mimetic, topoisomerase inhibitor, and RTK inhibitor.

62. The formulation of any one of claims 1-26 or the aqueous formulation of any one of claims 27-34 for use as a medicament.

63. The formulation of any one of claims 1-26 or the aqueous formulation of any one of claims 27-34 for use in a method of treating a cancer in a mammal.

64. The aqueous formulation for use of claim 63, wherein the aqueous formulation is to be administered intravenously.

65. The formulation for use of claim 63 or the aqueous formulation for use of claim 63 or 64, wherein the cancer is leukemia.

66. The formulation for use of claim 65 or the aqueous formulation for use of claim 65, wherein the leukemia is chronic lymphocytic leukemia, chronic myelocytic leukemia, acute lymphoblastic leukemia or acute myeloid leukemia.

67. The formulation for use of claims 62, 63 or 65 or the aqueous formulation for use of any one of claims 62-66, further comprising the formulation and the aqueous formulation to be administered in combination with a therapeutically effective amount of another second active agent or a supportive care therapy.

68. The formulation for use of claim 67 or the aqueous formulation for use of claim 67, wherein the other second active agent is a therapeutic antibody that specifically binds to a cancer antigen, hematopoietic growth factor, cytokine, anti-cancer agent, antibiotic, cox-2 inhibitor, immunomodulatory agent, immunosuppressive agent, corticosteroid or a pharmacologically active mutant or derivative thereof.

69. Compound 1 for use in a method of treating a leukemia in a mammal, wherein Compound 1 is (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof and wherein the Compound 1 is to be administered in combination with a second agent selected from a JAK inhibitor, a FLT3 inhibitor, an mTOR inhibitor, a spiceosome inhibitor, an ERK inhibitor, an LSD1 inhibitor, an SMG1 inhibitor, a BH3 mimetic, and a topoisomerase inhibitor to the mammal.

70. Compound 1 for use of claim 69, wherein the second agent is selected from pladienolide B, chloro-N,N-diethyl-5-((4-(2-(4-(3-methylureido)phenyl)pyridin-4-yl)pyrimidin-2-yl)amino)benzenesulfonamide (compound Ii), venetoclax, topotecan and everolimus.

71. Compound 1 for use of claim 69, wherein the second agent is a JAK inhibitor.

72. Compound 1 for use of claim 71, wherein the JAK inhibitor is selected from tofacitinib, momelotinib, filgotinib, decernotinib, barcitinib, ruxolitinib, fedratinib, NS-018 and pacritinib.

73. Compound 1 for use of claim 69, wherein the second agent is a FLT3 inhibitor.

74. Compound 1 for use of claim 73, wherein the FLT3 inhibitor is selected from quizartinib, sunitinib, midostaurin, pexidartinib, lestaurtinib, tandutinib, and crenolanib.

75. Compound 1 for use of claim 69, wherein the second agent is everolimus.

76. Compound 1 for use of any one of claims 69-75, wherein the leukemia is an acute myeloid leukemia.

77. Compound 1 for use of any one of claims 69-76, wherein the leukemia is relapsed, refractory or resistant.

78. Compound 1 for use in a method of treating a myeloproliferative neoplasm in a mammal, wherein Compound 1 is (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof and wherein the Compound 1 is to be administered in combination with a JAK inhibitor to the mammal.

79. Compound 1 for use of claim 78, wherein the JAK inhibitor is selected from tofacitinib, momelotinib, filgotinib, decernotinib, barcitinib, ruxolitinib, fedratinib, NS-018 and pacritinib.

80. Compound 1 for use in a method of treating a cancer selected from breast cancer, neuroendocrine tumor, and renal cell carcinoma in a mammal, wherein Compound 1 is (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof and wherein the Compound 1 is to be administered in combination with a second agent selected from everolimus, temsirolimus, 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one and 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((trans)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one to the mammal.

81. Compound 1 for use of claim 80, wherein the second agent is everolimus.

82. Compound 1 for use of any one of claims 69-81, wherein the formulation of any one of claims 1-26, or the aqueous formulation of any one of claims 27-34 is to be administered to the mammal.

83. Compound 1 for use in a method of treating a leukemia in a mammal, wherein Compound 1 is (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide), or a stereoisomer or mixture of stereoisomers, pharmaceutically acceptable salt, tautomer, prodrug, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, wherein the Compound 1 is to be administered in combination with an IDH2 inhibitor to the mammal and wherein the leukemia is characterized by the presence of a mutant allele of IDH2.

84. Compound 1 for use of claim 83, wherein the IDH2 inhibitor is enasidenib or 6-(6-(trifluoromethyl)pyridin-2-yl)-N^2-(2-(trifluoromethyl)pyridin-4-yl)-1,3,5-triazine-2,4-diamine.

85. Compound 1 for use of claim 83 or 84, wherein the leukemia is an acute myeloid leukemia characterized by the presence of a mutant allele of IDH2.

86. Compound 1 for use of any one of claims 83-85, wherein the leukemia is relapsed, refractory or resistant.

87. A process for preparing the formulation of any one of claims 1-11 comprising: dissolving (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide) in formic acid to obtain a premix, dissolving hydroxypropyl β-cyclodextrin in water to obtain a solution, adding the premix to the solution to obtain a drug solution.

88. The process of claim 89 further comprising lyophilizing the solution to produce a lyophilized formulation. A process for preparing the formulation of any one of claims 12-26 comprising: dissolving hydroxypropyl β-cyclodextrin in a citrate buffer to obtain a buffer solution, dissolving (2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-5-yl)methyl)-2,2-difluoroacetamide) in DMSO to obtain a premix, adding the premix to the buffer solution to obtain a solution.

89. The process of claim 87 further comprising lyophilizing the solution to produce a lyophilized formulation.