WHAT IS CLAIMED:

1. ~~A method of treating, preventing, managing, and/or ameliorating acute myeloid leukemia in a patient comprising administering to the patient a therapeutically effective amount of~~ Use of a compound 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 (Compound 1) in the manufacture of a medicament for treating acute myeloid leukemia, wherein the medicament is for administration in combination with 1) a therapeutically effective amount venetoclax and a therapeutically effective amount azacitidine or 2) a therapeutically effective amount a FLT3 inhibitor.

2. The ~~method~~use of claim 1~~ comprising administering a therapeutically effective amount of Compound 1,~~, wherein the medicament is for administration in combination with a therapeutically effective amount venetoclax and a therapeutically effective amount azacitidine.

3. The ~~method~~use of claim ~~1~~2, wherein the FLT3 inhibitor is gilteritinib.

4. The ~~method~~use of any one of claims 1-3, wherein the acute myeloid leukemia is refractory or relapsed acute myeloid leukemia.

5. The ~~method~~use of any one of claims 1-4, wherein the ~~therapeutically effective amount~~compound is to be administered in a dose of ~~Compound 1 is~~ about 0.1 mg to about 10 mg.

6. The ~~method~~use of any one of claims 1-5, wherein the ~~therapeutically effective amount of Compound 1~~dose is about 0.3 mg, 0.6 mg, 1.2 mg, 1.8 mg, 2 mg, 2.4 mg, 3 mg/day, 3.6 mg, 4.5 mg/day, 5.4 mg or 8.1 mg.

7. The ~~method~~use of any one of claims 1-2 and 5-6, wherein the therapeutically effective amount of venetoclax is about 400 mg.

8. The ~~method~~use of any one of claims 1-2 and 5-6, wherein the therapeutically effective amount of azacitidine is about 75 mg/m^2.

9. The ~~method~~use of any one of claims 1, 3 and 5-6, wherein the therapeutically effective amount of gilteritinib is about 120 mg.

10. The ~~method~~use of any one of claims 1-9, wherein the ~~method comprises~~compound is to be administered in one or more treatment cycles.

11. The ~~method~~use of claim 10, wherein each treatment cycle is a 28 day cycle.

12. The ~~method~~use of any one of claims 1-11, wherein Compound 1 is to be administered once daily on days 1 to 5 of the 28 day treatment cycle.

13. The ~~method~~use of any one of claims 1-~~11~~12, wherein Compound 1 is to be administered once daily on days 4 to 8 of the 28 day treatment cycle.

14. The ~~method~~use of claim 12 or 13, wherein the treatment cycle is to be repeated at least once.

15. The ~~method~~use of claim 14, wherein the treatment cycle is to be repeated 2 to 6 times.

16. The ~~method~~use of claim 1 or 2, wherein ~~the method comprises administering to the subject~~ Compound 1, venetoclax and azacitidine are to be administered in two or more 28 day cycles as follows:

in cycle 1~~ comprising administering,~~ 1.2 mg Compound 1 is to be administered once daily on days 4-8, 75 mg/m^2 azacitidine on days 1-7, 100 mg venetoclax on day 1, 200 mg venetoclax on day 2, and 400 mg venetoclax on days 3-28; and

in subsequent cycles~~ comprising administering,~~ 1.2 mg Compound 1 is to be administered once daily on days 1-5, 75 mg/m^2 azacitidine on days 1-7, and 400 mg venetoclax once daily on days 3-28.

17. The ~~method~~use of claim 1 or 2, wherein ~~the method comprises administering to the subject~~ Compound 1, venetoclax and azacitidine are to be administered in two or more 28 day cycles as follows:

in cycle 1~~ comprising administering,~~ 2 mg Compound 1 is to be administered once daily on days 4-8, 75 mg/m^2 azacitidine on days 1-7, 100 mg venetoclax on day 1, 200 mg venetoclax on day 2, and 400 mg venetoclax on days 3-28; and

in subsequent cycles~~ comprising administering,~~ 2 mg Compound 1 is to be administered once daily on days 1-5, 75 mg/m^2 azacitidine on days 1-7, and 400 mg venetoclax once daily on days 3-28.

18. The ~~method~~use of claim 1 or 2, wherein ~~the method comprises administering to the subject~~ Compound 1, venetoclax and azacitidine are to be administered in two or more 28 day cycles as follows:

in cycle 1 ~~comprising administering,~~ 3 mg Compound 1 is to be administered once daily on days 4-8, 75 mg/m^2 azacitidine on days 1-7, 100 mg venetoclax on day 1, 200 mg venetoclax on day 2, and 400 mg venetoclax on days 3-28; and

in subsequent cycles ~~comprising administering,~~ 3 mg Compound 1 is to be administered once daily on days 1-5, 75 mg/m^2 azacitidine on days 1-7, and 400 mg venetoclax once daily on days 3-28.

19. The ~~method~~use of claim 1 or 3, wherein the ~~method comprises administering to the subject~~ Compound 1 and gilteritinib are to be administered in one or more 28 day cycles, in each cycle ~~comprising administering~~ 1.2 mg Compound 1 is to be administered once daily on days 1-5 and 120 mg gilteritinib on days 1-28.

20. The ~~method~~use of claim 1 or 3, wherein the ~~method comprises administering to the subject~~ Compound 1 and gilteritinib are to be administered in one or more 28 day cycles, in each cycle ~~comprising administering~~ 2 mg Compound 1 is to be administered once daily on days 1-5 and 120 mg gilteritinib on days 1-28.

21. The ~~method~~use of claim 1 or 3, wherein ~~the method comprises administering to the subject~~ Compound 1 and gilteritinib are to be administered in one or more 28 day cycles, in each cycle ~~comprising administering~~ 3 mg Compound 1 is to be administered once daily on days 1-5 and 120 mg gilteritinib on days 1-28.

22. The ~~method~~use of any one of claims 1-21, wherein the ~~method comprises administering~~compound is to be administered with one or more of calcium, calcitriol, or vitamin D supplementation.

23. The ~~method~~use of any one of claims 1-~~22~~21, wherein ~~the method comprises administering~~ one or more of calcium, calcitriol, or vitamin D supplementation is to be administered prior to Compound 1.

24. The ~~method~~use of any one of claims 1-~~23~~21, wherein ~~the method comprises administering~~ one or more of calcium, calcitriol, or vitamin D supplementation are to be administered at least 3 days prior to Compound 1 on day 1 of the cycle.

25. The ~~method~~use of any one of claims 22-~~23~~24, wherein the patient does not have a disorder disrupting normal calcium homeostasis or preventing calcium supplementation.

~~26.~~ The ~~method~~use of any one of claims 1-~~25, further comprising administering a therapeutically effective amount of an additional active agent or a supportive care therapy.~~

~~27. The method of claim 26~~25, wherein the ~~additional active agent is selected from a group consisting of 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 and a therapeutic antibody that specifically binds to a cancer antigen.~~

~~28. The method of any one of claims 1-27, further comprising administering a second additional active agent selected from a group consisting of a glucocorticoid receptor agonist, an interleukin-1 receptor antagonist, an interleukin-1β blocker and a vasopressor.~~

~~29. A~~ compound ~~for use in a method of treating, preventing, managing, and/or ameliorating acute myeloid leukemia in a patient, wherein the method comprises administering to the patient a therapeutically effective amount 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 (Compound 1) in combination with 1) a therapeutically effective amount venetoclax and a therapeutically effective amount azacitidine or 2) a therapeutically effective amount a FLT3 inhibitor.~~

~~30. The compound for use in the method of claim 29, wherein method comprises administering a therapeutically effective amount of Compound 1, in combination with a therapeutically effective amount venetoclax and a therapeutically effective amount azacitidine.~~

~~31. The compound for use in the method of claim 29, wherein the FLT3 inhibitor is gilteritinib.~~

~~32. The compound for use in the method of any one of claims 29-31, wherein the acute myeloid leukemia is refractory or relapsed acute myeloid leukemia.~~

~~33. The compound for use in the method of any one of claims 29-32, wherein the therapeutically effective amount of Compound 1 is about 0.1 mg to about 10 mg.~~

~~34. The compound for use in the method of any one of claims 29-33, wherein the therapeutically effective amount of Compound 1 is about 0.3 mg, 0.6 mg, 1.2 mg, 1.8 mg, 2 mg, 2.4 mg, 3 mg/day, 3.6 mg, 4.5 mg/day, 5.4 mg or 8.1 mg.~~

~~35. The compound for use in the method of any one of claims 29-30 and 32-34, wherein the therapeutically effective amount of venetoclax is about 400 mg.~~

~~36. The compound for use in the method of any one of claims 29-30 and 32-34, wherein the therapeutically effective amount of azacitidine is about 75 mg/m^2.~~

~~37. The compound for use in the method of any one of claims 29, 31 and 32-34, wherein the therapeutically effective amount of gilteritinib is about 120 mg.~~

~~38. The compound for use in the method of any one of claims 29-37, wherein the method comprises one or more treatment cycles.~~

~~39. The compound for use in the method of claim 38, wherein each treatment cycle is a 28 day cycle.~~

~~40. The compound for use in the method of any one of claims 29-39, wherein Compound 1 is~~is be administered ~~once daily on days 1 to 5 of the 28 day treatment cycle.~~

~~41. The compound for use in the method of any one of claims 29-40, wherein Compound 1 is administered once daily on days 4 to 8 of the 28 day treatment cycle.~~

~~42. The compound for use in the method of claim 40 or 41, wherein the treatment cycle is repeated at least once.~~

~~43. The compound for use in the method of claim 42, wherein the treatment cycle is repeated 2 to 6 times.~~

~~44. The compound for use in the method of claim 29 or 30, wherein the method comprises administering to the subject Compound 1, venetoclax and azacitidine in two or more 28 day cycles as follows:~~

~~cycle 1 comprising administering 1.2 mg Compound 1 once daily on days 4-8, 75 mg/m^2 azacitidine on days 1-7, 100 mg venetoclax on day 1, 200 mg venetoclax on day 2, and 400 mg venetoclax on days 3-28; and~~

~~subsequent cycles comprising administering 1.2 mg Compound 1 once daily on days 1-5, 75 mg/m^2 azacitidine on days 1-7, and 400 mg venetoclax once daily on days 3-28.~~

~~45. The compound for use in the method of claim 29 or 30, wherein the method comprises administering to the subject Compound 1, venetoclax and azacitidine in two or more 28 day cycles as follows:~~

~~cycle 1 comprising administering 2 mg Compound 1 once daily on days 4-8, 75 mg/m^2 azacitidine on days 1-7, 100 mg venetoclax on day 1, 200 mg venetoclax on day 2, and 400 mg venetoclax on days 3-28; and~~

~~subsequent cycles comprising administering 2 mg Compound 1 once daily on days 1-5, 75 mg/m^2 azacitidine on days 1-7, and 400 mg venetoclax once daily on days 3-28.~~

~~46. The compound for use in the method of claim 29 or 30, wherein the method comprises administering to the subject Compound 1, venetoclax and azacitidine in two or more 28 day cycles as follows:~~

~~cycle 1 comprising administering 3 mg Compound 1 once daily on days 4-8, 75 mg/m^2 azacitidine on days 1-7, 100 mg venetoclax on day 1, 200 mg venetoclax on day 2, and 400 mg venetoclax on days 3-28; and~~

~~subsequent cycles comprising administering 3 mg Compound 1 once daily on days 1-5, 75 mg/m^2 azacitidine on days 1-7, and 400 mg venetoclax once daily on days 3-28.~~

~~47. The compound for use in the method of claim 29 or 31, wherein the method comprises administering to the subject Compound 1 and gilteritinib in one or more 28 day cycles, each cycle comprising administering 1.2 mg Compound 1 once daily on days 1-5 and 120 mg gilteritinib on days 1-28.~~

~~48. The compound for use in the method of claim 29 or 31, wherein the method comprises administering to the subject Compound 1 and gilteritinib in one or more 28 day cycles, each cycle comprising administering 2 mg Compound 1 once daily on days 1-5 and 120 mg gilteritinib on days 1-28.~~

~~49. The compound for use in the method of claim 29 or 31, wherein the method comprises administering to the subject Compound 1 and gilteritinib in one or more 28 day cycles, each cycle comprising administering 3 mg Compound 1 once daily on days 1-5 and 120 mg gilteritinib on days 1-28.~~

~~50. The compound for use in the method of any one of claims 29-49, wherein the method comprises administering one or more of calcium, calcitriol, or vitamin D supplementation.~~

~~51. The compound for use in the method of any one of claims 29-49, wherein the method comprises administering one or more of calcium, calcitriol, or vitamin D supplementation prior to Compound 1.~~

~~52. The compound for use in the method of any one of claims 29-49, wherein the method comprises administering one or more of calcium, calcitriol, or vitamin D supplementation at least 3 days prior to Compound 1 on day 1 of the cycle.~~

~~53. The compound for use in the method any one of claims 50-52, wherein the patient does not have a disorder disrupting normal calcium homeostasis or preventing calcium supplementation.~~

~~54.~~26. ~~The compound for use in the method of any one of claims 1-53, wherein the method further comprises administering~~further with a therapeutically effective amount of another additional active agent or a supportive care therapy.

~~55.~~27. The ~~compound for~~ use ~~in the method~~ of claim ~~54~~26, wherein the other additional active agent is selected from 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 and a therapeutic antibody that specifically binds to a cancer antigen.

~~56.~~28. The ~~compound for~~ use ~~in the method~~ of any one of claims 1-~~55~~27, wherein the ~~method comprises administering a~~ second additional active agent is selected from a group consisting of a glucocorticoid receptor agonist, an interleukin-1 receptor antagonist, an interleukin-1β blocker and a vasopressor.