WHAT IS CLAIMED IS:

1. Use of a combination of (i) a pharmaceutical composition comprising 5-azacytidine, (ii) at least one additional therapeutic agent, and (iii) a lysine specific demethylase-1 (LSD-1) inhibitor or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for ~~A method of~~ treating a human subject having acute myeloid leukemia (AML), wherein the ~~method comprises administering~~combination is to be administered to the subject ~~a combination of (i) a pharmaceutical composition comprising 5-azacytidine, (ii) at least one additional therapeutic agent, and (iii) a lysine specific demethylase-1 (LSD-1) inhibitor or a pharmaceutically acceptable salt thereof~~.

2. The ~~method~~ use of claim 1, wherein the subject is not eligible for intensive induction chemotherapy.

3. The use~~method~~ of claim 1, wherein:

(a) the 5-azacytidine and the at least one additional therapeutic agent are to be administered concomitantly; or

(b) the 5-azacytidine and the at least one additional therapeutic agent are to be administered sequentially wherein the 5-azacytidine is administered first.

4. The ~~method~~ use of claim 1, wherein:

(a) the 5-azacytidine and the at least one additional therapeutic agent are co-formulated as a single unit dosage form; or

(b) the 5-azacytidine and the at least one additional therapeutic agent are formulated as separate dosage forms.

5. The ~~method~~ use of claim 1, wherein:

(a) the 5-azacytidine and the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, are to be administered concomitantly; or

(b) the 5-azacytidine and the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, are to be administered sequentially.

6. The ~~method~~ use of claim 1, wherein:

(a) the 5-azacytidine, the at least one additional therapeutic agent, and the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, are to be administered concomitantly; or

(b) the 5-azacytidine, the at least one additional therapeutic agent, and the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, are to be administered sequentially.

7. The ~~method~~ use of claim 1, wherein the 5-azacytidine is to be administered:

(a) subcutaneously or intravenously; and/or

(b) at a dose of about 75 mg/m^2 to about 100 mg/m^2 subcutaneously or intravenously; and/or

(c) at a dose of about 75 mg/m^2 subcutaneously or intravenously; and/or

(d) subcutaneously or intravenously daily for the first seven days of a 28-day cycle.

~~.~~

8. The ~~method~~ use of claim 1, wherein the 5-azacytidine is to be administered:

(a) at a dose of about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, or 600 mg orally; and/or

(b) at a dose of about 200 mg; and/or

(c) at a dose of about 300 mg; and/or

(d) for the first seven, fourteen, or twenty-one days of a 28 day cycle; and/or

(e) to the human subject one or two times per day; and/or;

(f) in the form of a capsule or a tablet.

9. The ~~method~~ use of claim 8, wherein the 5-azacytidine is to be administered in the form of a non-enteric-coated tablet.

10. The ~~method~~ use of claim 1, wherein the 5-azacytidine is to be administered orally:

(a) at a dose of about 200 mg per day for 14 days in a 28-day cycle;

(b) at a dose of about 300 mg per day for 14 days in a 28-day cycle;

(c) at a dose of about 200 mg per day for 21 days in a 28-day cycle; or

(d) at a dose of about 300 mg per day for 21 days in a 28-day cycle.

11. The ~~method~~ use of claim 1, wherein the 5-azacytidine is to be administered orally:

(a) daily for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or greater than 14 days, optionally followed by a treatment dosing holiday of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or greater than 14 days;

(b) daily for 14 or more days, optionally followed by a treatment dosing holiday of 7 or more days;

(c) for 21 or more days, optionally followed by a treatment dosing holiday of 7 or more days;

(d) for 14 days, optionally followed by a treatment dosing holiday of 14 days;

(e) for 21 or more days, followed by a treatment dosing holiday of 7 or more days; or

(f) for 14 days, followed by a treatment dosing holiday of 14 days.

12. The ~~method~~ use of claim 1, wherein the 5-azacytidine is to be administered orally:

(a) at a dose of about 300 mg daily for 14 days, followed by a treatment dosing holiday of 14 days;

(b) at a dose of about 200 mg daily for 14 days, followed by a treatment dosing holiday of 14 days;

(c) at a dose of about 300 mg daily for 21 days, followed by a treatment dosing holiday of 7 days; or

(d) at a dose of about 200 mg daily, followed by a treatment dosing holiday of 7 days;

13. The ~~method~~ use of claim 1, wherein the 5-azacytidine is to be administered orally with:

(a) ~~using~~ a treatment cycle ~~comprising~~ wherein~~administration of~~ 5-azacytidine is to be administered per day for 7 days in a 28-day cycle;

(b) ~~using~~ a treatment cycle ~~comprising administration of~~ wherein 5-azacytidine is to be administered per day for 14 days in a 28-day cycle; or

(c) ~~using~~ a treatment cycle ~~comprising administration of~~wherein 5-azacytidine is to be administered per day for 21 days in a 28-day cycle.

14. The ~~method~~ use of claim 1, wherein the at least one additional therapeutic agent comprises gilteritinib, midostaurin, quizartinib, enasidenib, ivosidenib, and/or venetoclax.

15. The use~~method~~ of claim 14, wherein the at least one additional therapeutic agent is venetoclax.

16. The use~~method~~ of claim 15, wherein the venetoclax is to be administered:

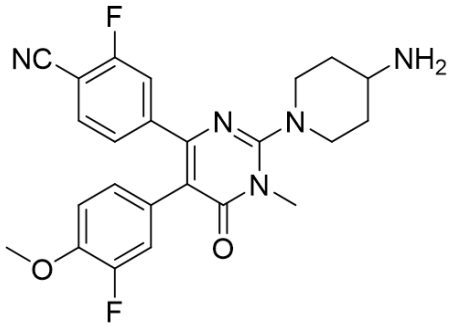
(a) orally; and/or

(b) in a form of a tablet; and/or

(c) daily; and/or

(d) at a dose of about 400 mg.

17. The use~~method~~ of claim 1, wherein the LSD-1 inhibitor is a compound having the structure:



or a pharmaceutically acceptable salt thereof.

18. The use~~method~~ of claim 17, wherein the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, is to be administered:

(a) orally; and/or

(b) in a form of a tablet or capsule; and/or

(c) once a week; and/or

(d) at a dose of about 20 mg, about 40 mg, or about 60 mg.

19. The use~~method~~ of claim 1, wherein:

(a) the AML is resistant to treatment with the 5-azacytidine alone; and/or

(b) the AML is resistant to treatment with the at least one additional therapeutic agent alone; and/or

(c) the AML is resistant to treatment with the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof alone; and/or

(d) the combination of the 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death as compared to the 5-azacytidine alone; and/or

(e) the combination of the 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death as compared to the 5-azacytidine alone by about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%; and/or

(f) the combination of the 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death as compared to at least one additional therapeutic agent alone; and/or

(g) the combination of the 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death as compared to the at least one additional therapeutic agent alone by about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%; and/or

(h) the combination of 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death as compared to the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof; and/or

(i) the combination of 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death as compared to the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof by about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%; and/or

(j) the combination of 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death compared to the combination of any two of 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof; and/or

(k) the combination of 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death compared to the combination of any two of 5-azacytidine, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof by about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%; and/or

(l) the 5-azacytidine administered orally and at least one additional therapeutic agent increases AML cell death as compared to 5-azacytidine administered intravenously or subcutaneously and at least one additional therapeutic agent; and/or

(m) the 5-azacytidine administered orally and at least one additional therapeutic agent increases AML cell death as compared to 5-azacytidine administered intravenously or subcutaneously and at least one additional therapeutic agent by about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about

55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%; and/or

(n) the combination of the 5-azacytidine administered orally, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death compared to the combination of the 5-azacytidine administered intravenously or subcutaneously, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof; and/or

(o) the combination of the 5-azacytidine administered orally, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof, increases AML cell death compared to the combination of the 5-azacytidine administered intravenously or subcutaneously, the at least one additional therapeutic agent, LSD-1 inhibitor, and a pharmaceutically acceptable salt thereof by about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100%.

20. The use~~method~~ of claim 1, wherein ~~the method comprises~~:

(a) ~~administering~~ the 5-azacytidine is to be administered subcutaneously or intravenously to the subject once daily for the first 7 days of a 28 day cycle;

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject once daily in a 28 day cycle; and

(c) ~~administering~~ the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, is to be administered to the subject once a week in a 28 day cycle.

21. The ~~method~~ use of claim 1, wherein ~~the method comprises~~:

(a) ~~administering~~ the 5-azacytidine is to be administered subcutaneously or intravenously to the subject on days 1, 2, 3, 4, 5, 6, and 7 days of a 28 day cycle;

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject on days 1,2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, and 28 of a 28 day cycle; and

(c) ~~administering~~ the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, is to be administered to the subject on days 1, 8, 15, and 22 of a 28 day cycle.

22. The use ~~method~~ of claim 21, ~~furthering comprising~~wherein:

(a) ~~administering~~ the 5-azacytidine at a dose of about 75 mg/m^2 is to be administered subcutaneously or intravenously every day for the first seven days of a 28 day cycle; and/or

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject at a dose of at least about 100 mg every day of a 28 day cycle; and/or

(c) ~~administering~~ the LSD-1 inhibitor is to be administered to the subject at a dose of about 20 mg, about 40 mg, or about 60 mg once a week of a 28 day cycle.

23. The ~~method~~ use of claim 22, wherein ~~the method comprises concurrently administering~~ the at least one additional therapeutic agent to the subject a dose of about 100 mg on Day 1, a dose of about 200 mg on Day 2, a dose of about 300 mg on Day 3, and a dose of about 400 mg on Days 4-28 of a 28 day cycle is to be concurrently administered.

24. The use ~~method~~ of claim 1, wherein ~~the method comprises~~:

(a) ~~administering~~ the 5-azacytidine at a dose of about 75 mg/m^2 is to be administered subcutaneously or intravenously every day for the first seven days of a 28 day cycle; and/or

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject at a dose of about 400 mg orally every day of a 28 day cycle; and/or

(c) ~~administering~~ the LSD-1 inhibitor is to be administered to the subject at a dose of about 20 mg, about 40 mg or about 60 mg orally once a week of a 28 day cycle.

25. The ~~method~~ use of claim 24, wherein ~~administering~~ the at least one additional therapeutic agent ~~comprises~~ to be administered comprises ~~administering~~ venetoclax.

26. The ~~method~~ use of claim 1, wherein ~~the method comprises the steps of~~:

(a) ~~administering~~ the 5-azacytidine is to be administered orally to the subject once daily for the first 14 days of a 28 day cycle;

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject once daily in a 28 day cycle; and

(c) ~~administering~~ the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, is to be administered to the subject once a week in a 28 day cycle.

27. The ~~method~~ use of claim 1, wherein ~~the method comprises the steps of~~:

(a) ~~administering~~ the 5-azacytidine is to be administered orally to the subject on days 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14 of a 28 day cycle;

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject on days 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, and 28 of a 28 day cycle; and

(c) ~~administering~~ the LSD-1 inhibitor, or a pharmaceutically acceptable salt thereof, is to be administered to the subject on days 1, 8, 15, and 22 of a 28 day cycle.

28. The ~~method~~ use of claim 27, ~~furthering comprising~~wherein:

(a) ~~administering~~ the 5-azacytidine is to be administered at a dose of about 300 mg every day for the first fourteen days of a 28 day cycle; and/or

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject at a dose of at least about 100 mg every day of a 28 day cycle; and/or

(c) ~~administering~~ the LSD-1 inhibitor is to be administered to the subject at a dose of about 20 mg, about 40 mg, or about 60 mg once a week of a 28 day cycle.

29. The ~~method~~ use of claim 28, wherein ~~the method comprises concurrently administering~~ the at least one additional therapeutic agent is to be concurrently administered to the subject a dose of about 100 mg on Day 1, a dose of about 200 mg on Day 2, a dose of about 300 mg on Day 3, and a dose of about 400 mg on Days 4-28 of a 28 day cycle.

30. The ~~method~~ use of claim 1, wherein ~~the method comprises~~:

(a) ~~administering~~ the 5-azacytidine is to be administered at a dose of about 300 mg orally every day for the first fourteen days of a 28 day cycle; and/or

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject at a dose of about 400 mg orally every day of a 28 day cycle; and/or

(c) ~~administering~~ the LSD-1 inhibitor is to be administered to the subject at a dose of about 20 mg, about 40 mg or about 60 mg orally once a week of a 28 day cycle.

31. The ~~method~~ use of claim 30, wherein ~~administering~~ the at least one additional therapeutic agent to be administered comprises ~~administering~~ venetoclax.

32. The ~~method~~ use of claim 27, ~~furthering comprising~~ wherein:

(a) ~~administering~~ the 5-azacytidine is to be administered at a dose of about 200 mg every day for the first fourteen days of a 28 day cycle; and/or

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject at a dose of at least about 100 mg every day of a 28 day cycle; and/or

(c) ~~administering~~ the LSD-1 inhibitor is to be administered to the subject at a dose of about 20 mg, about 40 mg, or about 60 mg once a week of a 28 day cycle.

33. The ~~method~~ use of claim 32, wherein ~~the method comprises concurrently administering~~ the at least one additional therapeutic agent is to be concurrently administered to the subject a dose of about 100 mg on Day 1, a dose of about 200 mg on Day 2, a dose of about 300 mg on Day 3, and a dose of about 400 mg on Days 4-28 of a 28 day cycle.

34. The ~~method~~ use of claim 1, wherein ~~the method comprises~~:

(a) ~~administering~~ the 5-azacytidine is to be administered at a dose of about 200 mg orally every day for the first fourteen days of a 28 day cycle; and/or

(b) ~~administering~~ the at least one additional therapeutic agent is to be administered to the subject at a dose of about 400 mg orally every day of a 28 day cycle; and/or

(c) ~~administering~~ the LSD-1 inhibitor is to be administered to the subject at a dose of about 20 mg, about 40 mg or about 60 mg orally once a week of a 28 day cycle.

35. The ~~method~~ use of claim 34, wherein ~~administering~~ the at least one additional therapeutic agent to be administered comprises ~~administering~~ venetoclax.

36. The ~~method~~ use of claim 1, wherein the acute myeloid leukemia comprises acute myeloid leukemia with recurrent genetic abnormalities, acute myeloid leukemia with myelodysplasia-related changes, therapy-related myeloid neoplasms, myeloid sarcoma, myeloid proliferations related to Down syndrome, blastic plasmacytoid dendritic cell neoplasm, and/or acute promyelocytic leukaemia.

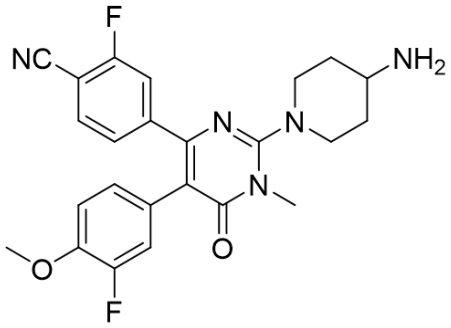
37. Use of 5-azacytidine, venetoclax and a pharmaceutical composition in the manufacture of a medicament for~~A method of~~ treating a human subject having acute myeloid leukemia (AML) who is not eligible for intensive induction chemotherapy, wherein the medicament is to be administered ~~the method comprises administering~~ to the human subject:

(i) in a first continuous 28-day cycle:

(a) the 5-azacytidine subcutaneously or intravenously daily at a dose of about 75 mg/m^2 on Days 1 to 7;

(b) the venetoclax orally at a dose of about 100 mg on Day 1; about 200 mg on Day 2, and about 400 mg daily on Days 3 to 28; and

(c) the~~a~~ pharmaceutical composition comprising the besylate salt of the following compound:



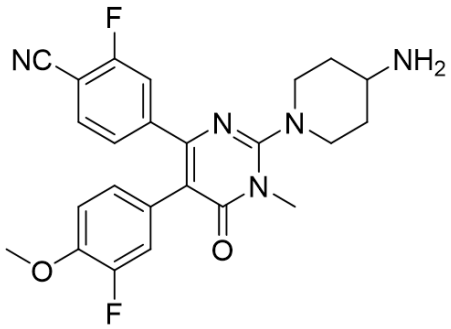
on Days 1, 8, 15, and 22; and

(ii) in subsequent 28 day cycles:

(d) the 5-azacytidine subcutaneously or intravenously daily at a dose of about 75 mg/m^2 on Days 1 to 7 of each subsequent cycle;

(e) the venetoclax orally at a dose of about 400 mg on Days 1 to 28 of each subsequent cycle; and

(f) the~~a~~ pharmaceutical composition comprising the besylate salt of the following compound



on Days 1, 8, 15, and 22 of each subsequent cycle.

38. The ~~method~~ use of claim 37, wherein the pharmaceutical composition is to be administered at:

(a) the dose of about 20 mg in the first continuous 28-day cycle and subsequent 28 day cycles;

(b) the dose of about 40 mg in the first continuous 28-day cycle and subsequent 28 day cycles; or

(c) the dose of about 60 mg in the first continuous 28-day cycle and subsequent 28 day cycles.

39. The ~~method~~ use of claim 38, wherein the pharmaceutical composition is to be administered at the dose of about 20 mg in the first continuous 28-day cycle and subsequent 28 day cycles; and if the dose of 20 mg is tolerated, then a second dose cohort will open where the pharmaceutical composition is to be administered at the dose of about 40 mg in the first continuous 28-day cycle and subsequent 28 day cycles.

40. The ~~method~~ use of claim 39, wherein if the dose of 40 mg is tolerated, then a third dose cohort will open where the pharmaceutical composition is to be administered at the dose of about 40 mg in the first continuous 28-day cycle and subsequent 28 day cycles.