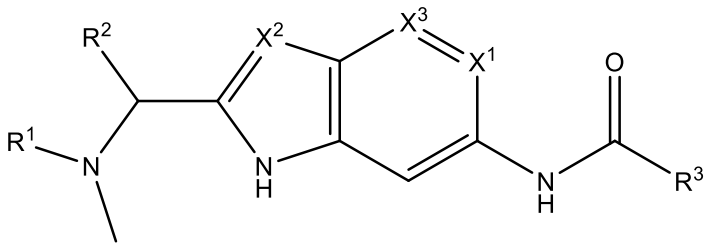
## CLAIMS

1. A compound of Formula I:




**Formula I**

wherein:

$X^1$, $X^2$, and $X^3$ are independently chosen from N and CH;

$R^1$ and $R^2$ are chosen from:

(a) $R^1$ and $R^2$ taken together form a pyrrolidine or piperidine; and

(b) $R^1$ and $R^2$ are methyl;

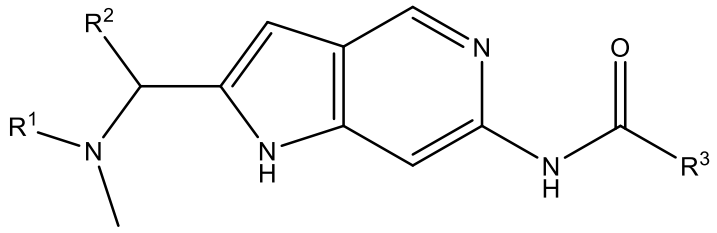
$R^3$ is a fused bicycle selected from:

(a) a fused 5,6 bicyclic heterocycle, optionally substituted with one or more $C_1$-$C_6$ alkyl (methyl);

(b) a fused 6,5 bicyclic heterocycle, optionally substituted with one or more of the following: $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl, $C_3$-$C_8$ carbocycle, $C_1$-$C_6$ oxaalkyl, $C_1$-$C_6$ alkoxy, oxo, halogen, heterocycle, and $NHR^4$, where $R^4$ is chosen from $C_1$-$C_6$ alkyl and $C_1$-$C_6$ oxaalkyl; and

(c) a fused 6,6 bicyclic heterocycle, optionally substituted with one or more of the following: $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, halogen, and $NHR^5$, wherein $R^5$ is chosen from hydrogen and $C_1$-$C_6$ alkyl.

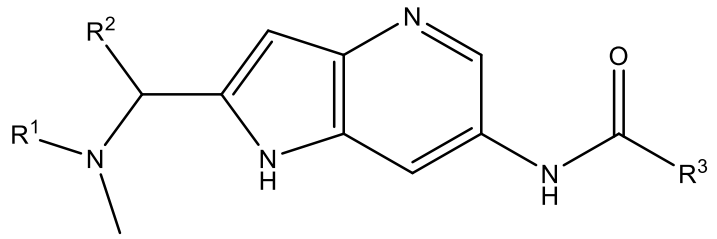
2. A compound according to claim 1 of Formula II:



**Formula II**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

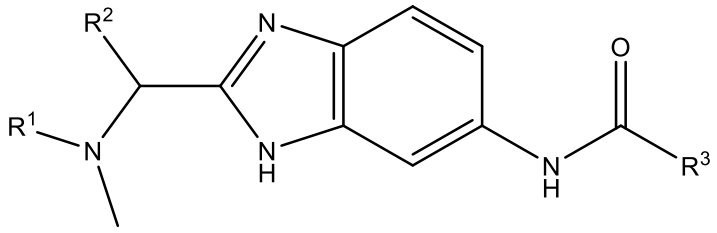
3. A compound according to claim 1 of Formula III:



**Formula III**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

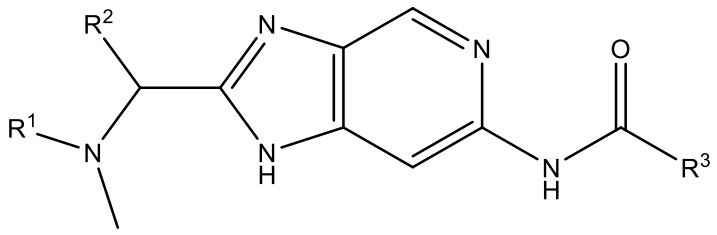
4. A compound according to claim 1 of Formula IV:



**Formula IV**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

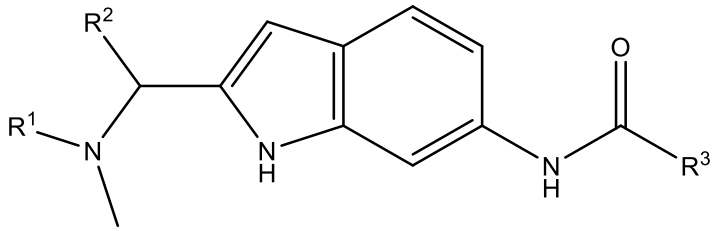
5. A compound according to claim 1 of Formula V:



**Formula V**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

6. A compound according to claim 1 of Formula VI



**Formula VI**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

7. A pharmaceutical composition comprising a compound of any of claims 1-6 and one or more pharmaceutically acceptable carriers.

8. The pharmaceutical composition of claim 7, further comprising one or more therapeutic agents.

9. The pharmaceutical composition of claim 8, wherein the one or more therapeutic agent is selected from the group consisting of Bcl-2 inhibitors, cyclin-dependent kinase 4 and 6 (CDK 4/6 inhibitors), DNA methyltransferase inhibitors, histone deacetylase (HDAC) inhibitors, mTOR inhibitors, mutant isocitrate dehydrogenase (IDH1 and IDH2) inhibitors, glucocorticoids, an epigenetic modulators and chemotherapeutic agents.

10. Use of a therapeutically effective amount of a compound of any of claims 1-6 or a pharmaceutical composition of claims 7-9 in the manufacture of a medicament for the

treatment of acute leukemia wherein the medicament is to be administered to a subject in need thereof.

11. The use of claim 10, wherein the acute leukemia is acute lymphoblastic leukemia (ALL).

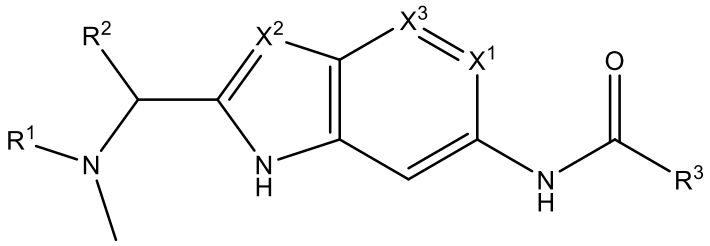
12. The use of claim 10, wherein the acute leukemia is acute myelogenous leukemia (AML).

13. The use of claim 12, wherein the AML is a subtype selected from the group consisting of acute myeloid leukemia, minimally differentiated (MO), acute myeloid leukemia without maturation (M1), acute myeloid leukemia with maturation (M2), acute myeloid leukemia with maturation with t(8;21), acute promyelocytic leukemia (M3), hypergranular type, microgranular type, acute myelomonocytic leukemia (M4), acute myelomonocytic leukemia with increased marrow eosinophils (M4E0), acute monocytic leukemia (M5), acute monoblastic leukemia (M5a), acute monocytic leukemia with maturation (M5b), erythroleukemia erythroid /myeloid (M6a), pure erythroid malignancy (M6b), acute megakaryoblastic leukemia (M7), acute megakaryoblastic leukemia associated with t(1;22), acute basophilic leukemia, acute myelofibrosis (acute myelodysplasia with myelofibrosis), acute leukemia and transient myeloproliferative disorder in Down's Syndrome, hypocellular acute myeloid leukemia, and myeloid sarcoma.

14. The use of claim 10, wherein the at least one compound is to be administered orally.

15. The use of claim 10, wherein the at least one compound is to be administered from one to four times per day.

16. A compound of Formula I:




**Formula I**

wherein:

$X^1$, $X^2$, and $X^3$ are independently chosen from N and CH;

$R^1$ and $R^2$ are chosen from:

(a) $R^1$ and $R^2$ taken together form a pyrrolidine or piperidine; and

(b) $R^1$ and $R^2$ are methyl;

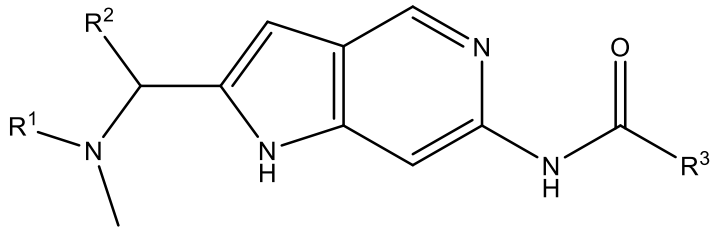
$R^3$ is a fused bicycle selected from:

(a) a fused 5,6 bicyclic heterocycle, optionally substituted with one or more $C_1$-$C_6$ alkyl (methyl);

(b) a fused 6,5 bicyclic heterocycle, optionally substituted with one or more of the following: $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl, $C_3$-$C_8$ carbocycle, $C_1$-$C_6$ oxaalkyl, $C_1$-$C_6$ alkoxy, oxo, halogen, heterocycle, and $NHR^4$, where $R^4$ is chosen from $C_1$-$C_6$ alkyl and $C_1$-$C_6$ oxaalkyl; and

(c) a fused 6,6 bicyclic heterocycle, optionally substituted with one or more of the following: $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, halogen, oxo, and $NHR^5$, wherein $R^5$ is chosen from hydrogen and $C_1$-$C_6$ alkyl.

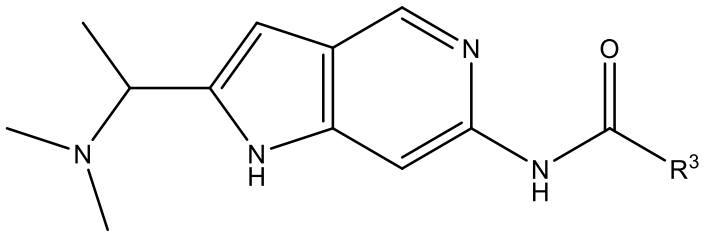
17. A compound according to claim 16 of Formula II:



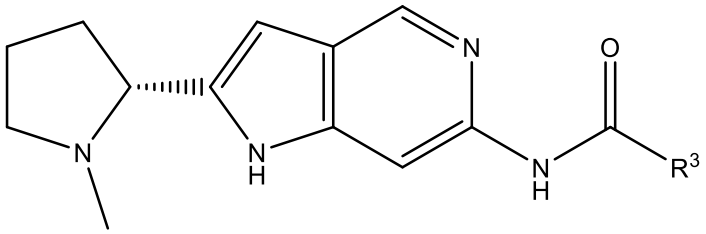

**Formula II**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

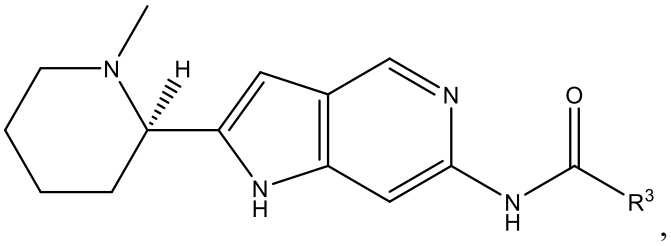
18. A compound according to claim 17 of Formula IIa, IIb or IIc:



**Formula IIa**



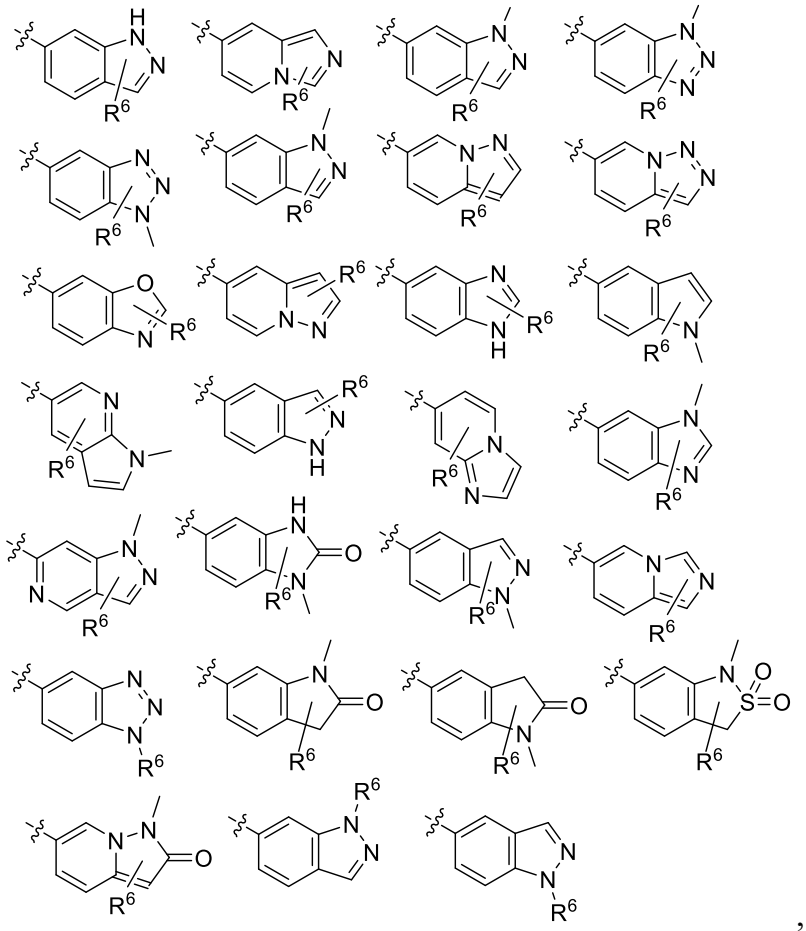
**Formula IIb**



**Formula IIc**

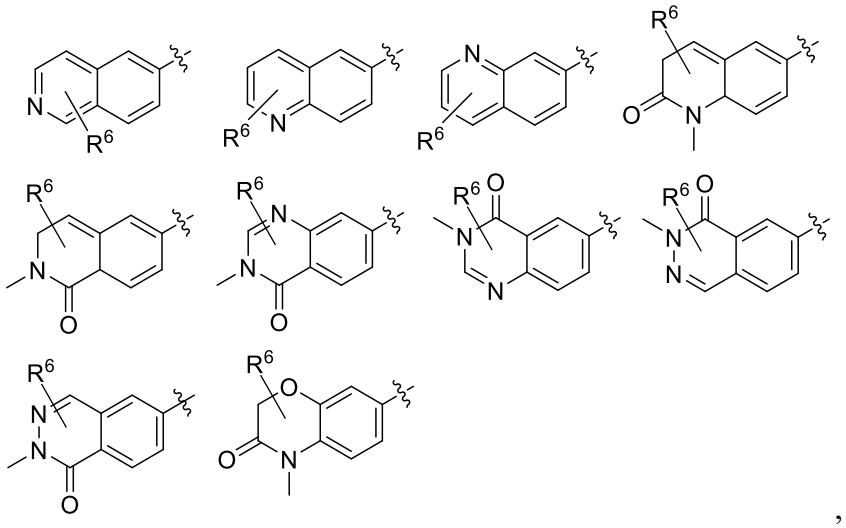
wherein $R^3$ is defined as above for Formula I.

19. A compound according to claim 18, wherein $R^3$ is a fused 6,5 bicyclic heterocycle selected from the following



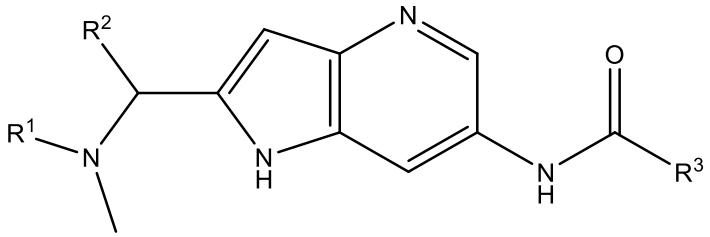
optionally substituted with one or more $R^6$ selected from the group consisting of: $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl, $C_3$-$C_8$ carbocycle, $C_1$-$C_6$ oxaalkyl, $C_1$-$C_6$ alkoxy, oxo, halogen, heterocycle, and $NHR^4$, where $R^4$ is chosen from $C_1$-$C_6$ alkyl and $C_1$-$C_6$ oxaalkyl.

20. A compound according to claim 18, wherein $R^3$ is a fused 6,6 bicyclic heterocycle selected from the following



optionally substituted with one or more $R^6$: $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, halogen, oxo, and $NHR^5$, wherein $R^5$ is chosen from hydrogen and $C_1$-$C_6$ alkyl.

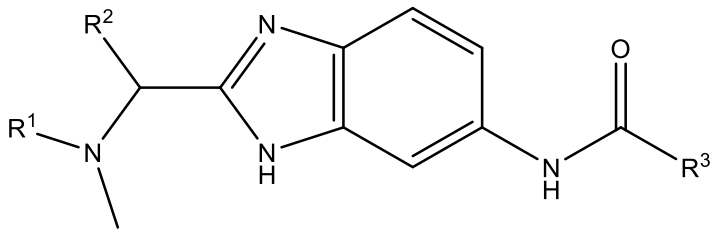
21. A compound according to claim 16 of Formula III:



**Formula III**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

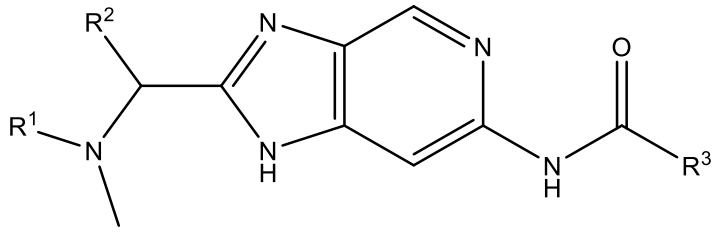
22. A compound according to claim 16 of Formula IV:



**Formula IV**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

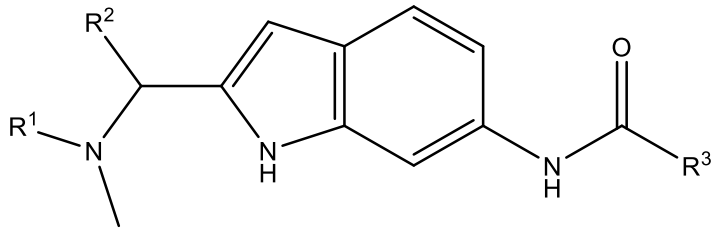
23. A compound according to claim 16 of Formula V:



**Formula V**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

24. A compound according to claim 16 of Formula VI



**Formula VI**

wherein $R^1$, $R^2$ and $R^3$ are as defined above for Formula I.

25. A pharmaceutical composition comprising a compound of any of claims 16-24 and one or more pharmaceutically acceptable carriers.

26. The pharmaceutical composition of claim 25, further comprising one or more therapeutic agents.

27. The pharmaceutical composition of claim 26, wherein the one or more therapeutic agent is selected from the group consisting of Bcl-2 inhibitors, cyclin-dependent kinase 4 and 6 (CDK 4/6 inhibitors), DNA methyltransferase inhibitors, histone deacetylase (HDAC) inhibitors, mTOR inhibitors, mutant isocitrate dehydrogenase (IDH1 and IDH2) inhibitors, glucocorticoids, an epigenetic modulators and chemotherapeutic agents.

28. Use of a therapeutically effective amount of a compound of any of claims 16-24 or a pharmaceutical composition of claims 25-27 in the manufacture of a medicament for

treating an acute leukemia wherein the medicament is to be administered to a subject in need thereof.

29. The use of claim 28, wherein the acute leukemia is acute lymphoblastic leukemia (ALL).

30. The use of claim 28, wherein the acute leukemia is acute myelogenous leukemia (AML).

31. The use of claim 30, wherein the AML is a subtype selected from the group consisting of acute myeloid leukemia, minimally differentiated (MO), acute myeloid leukemia without maturation (M1), acute myeloid leukemia with maturation (M2), acute myeloid leukemia with maturation with t(8;21), acute promyelocytic leukemia (M3), hypergranular type, microgranular type, acute myelomonocytic leukemia (M4), acute myelomonocytic leukemia with increased marrow eosinophils (M4E0), acute monocytic leukemia (M5), acute monoblastic leukemia (M5a), acute monocytic leukemia with maturation (M5b), erythroleukemia erythroid /myeloid (M6a), pure erythroid malignancy (M6b), acute megakaryoblastic leukemia (M7), acute megakaryoblastic leukemia associated with t(1;22), acute basophilic leukemia, acute myelofibrosis (acute myelodysplasia with myelofibrosis), acute leukemia and transient myeloproliferative disorder in Down's Syndrome, hypocellular acute myeloid leukemia, and myeloid sarcoma.

32. The use of claim 28, wherein the at least one compound is to be administered orally.

33. The use of claim 28, wherein the at least one compound is to be administered from one to four times per day.