

R¹ is selected from R⁵⁰;

R² is selected from R⁵⁰;

R³ is selected from hydrogen, halogen, -OH, -N(R⁵²)₂, -CN, -C(O)OR⁵², C₁₋₃alkyl, and C₁₋₃haloalkyl;

R^A, R^B and R^C are each independently selected at each occurrence from R⁵⁰, or two R^A groups, two R^B groups or two R^C groups attached to the same atom or different atoms can together optionally form a bridge or ring;

m, n and p are each independently an integer from 0 to 6;

R⁵⁰ is independently selected at each occurrence from:

halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²);

C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl, each of which is independently optionally substituted at each occurrence with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₃₋₁₂ carbocycle, and 3- to 12-membered heterocycle; and

C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle,

wherein each C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle in R⁵⁰ is independently optionally substituted with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl;

R⁵¹ is independently selected at each occurrence from:

hydrogen, -C(O)R⁵², -C(O)OR⁵², -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴;

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is independently optionally substituted at each occurrence with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -

$P(O)(OR^{52})_2$, $-P(O)(R^{52})_2$, $=O$, $=S$, $=N(R^{52})$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; and

further wherein R^{56} optionally forms a bond to ring C; and

R^{59} is independently selected at each occurrence from C_{1-20} alkyl, C_{2-20} alkenyl, C_{2-20} alkynyl, 1- to 6-membered heteroalkyl, C_{3-12} carbocycle, and 3- to 12-membered heterocycle, each of which is optionally substituted by halogen, $-CN$, $-NO_2$, $-NH_2$, $-NHCH_3$, $-NHCH_2CH_3$, $=O$, $-OH$, $-OCH_3$, $-OCH_2CH_3$, C_{3-12} carbocycle, or 3- to 6-membered heterocycle, wherein for a compound or salt of Formula (II-A), when R^{56} is $-CH_3$, L^3 is not further substituted with $-OH$, $-NH_2$, or $-CN$.

[0031b] In certain aspects, the present disclosure provides a pharmaceutical composition comprising a compound as described herein and a pharmaceutically acceptable carrier.

[0031c] In certain aspects, the present disclosure provides a use of a compound or salt as described herein in the manufacture of a medicament for the treatment of leukemia, a hematologic malignancy, a solid tumor cancer, prostate cancer, breast cancer, liver cancer, a brain tumor, or diabetes.

INCORPORATION BY REFERENCE

[0032] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0034] FIG. 1 is an amino acid sequence of human menin, isoform 1 (SEQ ID NO: 1).

[0035] FIG. 2 is an amino acid sequence of human menin, isoform 2 (SEQ ID NO: 2).

[0036] FIG. 3 is an amino acid sequence of human menin, isoform 3 (SEQ ID NO: 3).

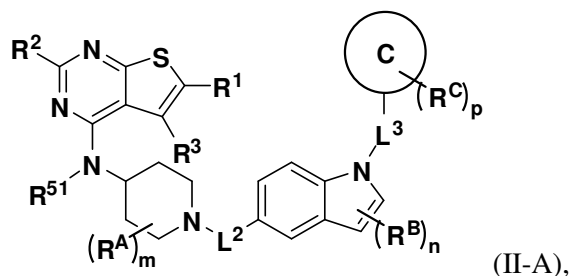
[0037] FIG. 4 depicts the change in volume of MV4;11 tumors in vehicle and compound treated mice.

[0038] FIG. 5 depicts the luminescence of MV4;11-luc tumors in vehicle and compound treated xenotransplantation mouse models of MLL leukemia after 6 days of treatment.

CLAIMS

What is claimed is:

1. A compound of Formula (II-A):



or a pharmaceutically acceptable salt thereof, wherein:

C is selected from C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle;

L² is selected from bond, -O-, -S-, -N(R⁵¹)-, -N(R⁵¹)CH₂-, -C(O)-, -C(O)O-, -OC(O)-, -OC(O)O-, -C(O)N(R⁵¹)-, -C(O)N(R⁵¹)C(O)-, -C(O)N(R⁵¹)C(O)N(R⁵¹)-, -N(R⁵¹)C(O)-, -N(R⁵¹)C(O)N(R⁵¹)-, -N(R⁵¹)C(O)O-, -OC(O)N(R⁵¹)-, -C(NR⁵¹)-, -N(R⁵¹)C(NR⁵¹)-, -C(NR⁵¹)N(R⁵¹)-, -N(R⁵¹)C(NR⁵¹)N(R⁵¹)-, -S(O)₂-, -OS(O)-, -S(O)O-, -S(O)-, -OS(O)₂-, -S(O)₂O-, -N(R⁵¹)S(O)₂-, -S(O)₂N(R⁵¹)-, -N(R⁵¹)S(O)-, -S(O)N(R⁵¹)-, -N(R⁵¹)S(O)₂N(R⁵¹)-, -N(R⁵¹)S(O)N(R⁵¹)-; alkylene, alkenylene, alkynylene, heteroalkylene, heteroalkenylene, and heteroalkynylene, each of which is optionally substituted with one or more R⁵⁰;

L³ is selected from alkylene, alkenylene, and alkynylene, each of which is substituted with one or more R⁵⁶ and optionally further substituted with one or more R⁵⁰;

R¹ is selected from R⁵⁰;

R² is selected from R⁵⁰;

R³ is selected from hydrogen, halogen, -OH, -N(R⁵²)₂, -CN, -C(O)OR⁵², C₁₋₃alkyl, and C₁₋₃haloalkyl;

R^A, R^B and R^C are each independently selected at each occurrence from R⁵⁰, or two R^A groups, two R^B groups or two R^C groups attached to the same atom or different atoms can together optionally form a bridge or ring;

m, n and p are each independently an integer from 0 to 6;

R⁵⁰ is independently selected at each occurrence from:

halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²);

C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl, each of which is independently optionally substituted at each occurrence with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₃₋₁₂ carbocycle, and 3- to 12-membered heterocycle; and

C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle,

wherein each C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle in R⁵⁰ is independently optionally substituted with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl;

R⁵¹ is independently selected at each occurrence from:

hydrogen, -C(O)R⁵², -C(O)OR⁵², -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴;

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is independently optionally substituted at each occurrence with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle; and

C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle,

wherein each C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle in R⁵¹ is independently optionally substituted with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle; and

NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl;

R⁵² is independently selected at each occurrence from hydrogen; and C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₂₋₂₀ alkynyl, 1- to 6-membered heteroalkyl, C₃₋₁₂ carbocycle, and 3- to 12-membered heterocycle, each of which is optionally substituted by halogen, -CN, -NO₂, -NH₂, -NHCH₃, -NHCH₂CH₃, =O, -OH, -OCH₃, -OCH₂CH₃, C₃₋₁₂ carbocycle, or 3- to 6-membered heterocycle;

R⁵³ and R⁵⁴ are taken together with the nitrogen atom to which they are attached to form a heterocycle, optionally substituted with one or more R⁵⁰;

R⁵⁶ is independently selected at each occurrence from:

-NO₂, -OR⁵⁹, -SR⁵², -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, C₂₋₁₀ alkynyl, C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle,

wherein each C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl in R⁵⁶ is independently optionally substituted at each occurrence with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵⁹, -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₃₋₁₂ carbocycle, and 3- to 12-membered heterocycle;

wherein each C₃₋₁₂ carbocycle and 3- to 12-membered heterocycle in R⁵⁶ is independently optionally substituted with one or more substituents selected from halogen, -NO₂, -CN, -OR⁵², -SR⁵², -N(R⁵²)₂, -NR⁵³R⁵⁴, -S(=O)R⁵², -S(=O)₂R⁵², -S(=O)₂N(R⁵²)₂, -S(=O)₂NR⁵³R⁵⁴, -NR⁵²S(=O)₂R⁵², -NR⁵²S(=O)₂N(R⁵²)₂, -NR⁵²S(=O)₂NR⁵³R⁵⁴, -C(O)R⁵², -C(O)OR⁵², -OC(O)R⁵², -OC(O)OR⁵², -OC(O)N(R⁵²)₂, -OC(O)NR⁵³R⁵⁴, -NR⁵²C(O)R⁵², -NR⁵²C(O)OR⁵², -NR⁵²C(O)N(R⁵²)₂, -NR⁵²C(O)NR⁵³R⁵⁴, -C(O)N(R⁵²)₂, -C(O)NR⁵³R⁵⁴, -P(O)(OR⁵²)₂, -P(O)(R⁵²)₂, =O, =S, =N(R⁵²), C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl; and

further wherein R⁵⁶ optionally forms a bond to ring C; and

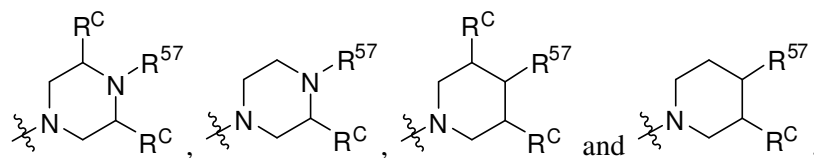
R^{59} is independently selected at each occurrence from C_{1-20} alkyl, C_{2-20} alkenyl, C_{2-20} alkynyl, 1- to 6-membered heteroalkyl, C_{3-12} carbocycle, and 3- to 12-membered heterocycle, each of which is optionally substituted by halogen, -CN, -NO₂, -NH₂, -NHCH₃, -NHCH₂CH₃, =O, -OH, -OCH₃, -OCH₂CH₃, C_{3-12} carbocycle, or 3- to 6-membered heterocycle,

wherein for a compound or salt of Formula (II-A), when R^{56} is -CH₃, L^3 is not further substituted with -OH, -NH₂, or -CN.

2. The compound of claim 1, wherein R^C is selected from -C(O) R^{52} , -S(=O) R^{52} , -S(=O)₂ R^{52} , -S(=O)₂N(R^{52})₂, -S(=O)₂NR⁵³ R^{54} , -NR⁵²S(=O)₂ R^{52} , =O, C_{1-3} alkyl, and C_{1-3} haloalkyl, or two R^C groups attached to different atoms can together form a C_{1-3} bridge.

3. The compound of claim 1 or 2, wherein C is 5- to 12-membered saturated heterocycle, wherein the heterocycle comprises at least one nitrogen atom.

4. The compound of claim 1, wherein C is selected from:



wherein R^{57} is selected from -S(=O) R^{52} , -S(=O)₂ R^{52} , -S(=O)₂N(R^{52})₂, -S(=O)₂NR⁵³ R^{54} , -NR⁵²S(=O)₂ R^{52} ; and C_{1-10} alkyl substituted with one or more substituents selected from -S(=O) R^{52} , -S(=O)₂ R^{52} , -S(=O)₂N(R^{52})₂, -S(=O)₂NR⁵³ R^{54} , and -NR⁵²S(=O)₂ R^{52} .

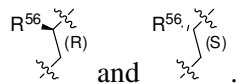
5. The compound of any one of the preceding claims, wherein R^1 is C_{1-3} haloalkyl.

6. The compound of any one of the preceding claims, wherein m is 0 and n is an integer from 1 to 3.

7. The compound of any one of the preceding claims, wherein L^2 is C_{1-4} alkylene, optionally substituted with one or more R^{50} .

8. The compound of any one of the preceding claims, wherein L^3 is substituted with =O, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-3} alkyl(cyclopropyl), C_{1-3} alkyl(NR⁵²C(O) R^{52}) or -O(C_{1-6} alkyl).

9. The compound of any one of claims 1 to 9, wherein L^3 is selected from



10. The compound of claim 9, wherein R^{56} is methyl.

11. The compound of claim 1, wherein:

L^2 is selected from -O-, -S-, -NH-, and -CH₂-;

L^3 is selected from C_{1-6} alkylene, C_{2-6} alkenylene, and C_{2-6} alkynylene, each of which is substituted with one or more R^{56} and optionally further substituted with one or more R^{50} ;

R^A , R^B and R^C are each independently selected at each occurrence from R^{50} , or two R^A groups, two R^B groups or two R^C groups attached to the same atom or different atoms can together optionally form a bridge or ring;

m is an integer from 0 to 3;

n is an integer from 1 to 3;

p is an integer from 0 to 6;

R^{56} is independently selected at each occurrence from:

$-OR^{59}$, $=O$, C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl,

wherein each C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl in R^{56} is independently optionally substituted at each occurrence with one or more substituents selected from halogen, $-NO_2$, $-CN$, $-OR^{59}$, $-SR^{52}$, $-N(R^{52})_2$, $-NR^{53}R^{54}$, $-S(=O)R^{52}$, $-S(=O)_2R^{52}$, $-S(=O)_2N(R^{52})_2$, $-S(=O)_2NR^{53}R^{54}$, $-NR^{52}S(=O)_2R^{52}$, $-NR^{52}S(=O)_2N(R^{52})_2$, $-NR^{52}S(=O)_2NR^{53}R^{54}$, $-C(O)R^{52}$, $-C(O)OR^{52}$, $-OC(O)R^{52}$, $-OC(O)OR^{52}$, $-OC(O)N(R^{52})_2$, $-OC(O)NR^{53}R^{54}$, $-NR^{52}C(O)R^{52}$, $-NR^{52}C(O)OR^{52}$, $-NR^{52}C(O)N(R^{52})_2$, $-NR^{52}C(O)NR^{53}R^{54}$, $-C(O)N(R^{52})_2$, $-C(O)NR^{53}R^{54}$, $-P(O)(OR^{52})_2$, $-P(O)(R^{52})_2$, $=O$, $=S$, $=N(R^{52})$, C_{3-12} carbocycle, and 3- to 12-membered heterocycle;

wherein each C_{3-12} carbocycle and 3- to 12-membered heterocycle in R^{56} is independently optionally substituted with one or more substituents selected from halogen, $-NO_2$, $-CN$, $-OR^{52}$, $-SR^{52}$, $-N(R^{52})_2$, $-NR^{53}R^{54}$, $-S(=O)R^{52}$, $-S(=O)_2R^{52}$, $-S(=O)_2N(R^{52})_2$, $-S(=O)_2NR^{53}R^{54}$, $-NR^{52}S(=O)_2R^{52}$, $-NR^{52}S(=O)_2N(R^{52})_2$, $-NR^{52}S(=O)_2NR^{53}R^{54}$, $-C(O)R^{52}$, $-C(O)OR^{52}$, $-OC(O)R^{52}$, $-OC(O)OR^{52}$, $-OC(O)N(R^{52})_2$, $-OC(O)NR^{53}R^{54}$, $-NR^{52}C(O)R^{52}$, $-NR^{52}C(O)OR^{52}$, $-NR^{52}C(O)N(R^{52})_2$, $-NR^{52}C(O)NR^{53}R^{54}$, $-C(O)N(R^{52})_2$, $-C(O)NR^{53}R^{54}$, $-P(O)(OR^{52})_2$, $-P(O)(R^{52})_2$, $=O$, $=S$, $=N(R^{52})$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; and

further wherein R^{56} optionally forms a bond to ring C; and

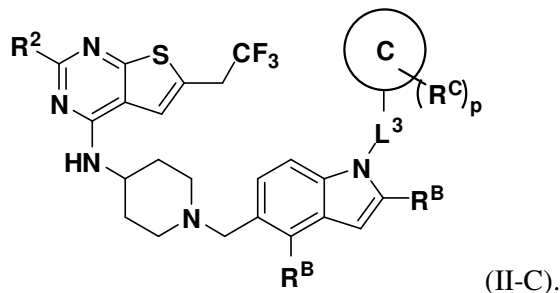
R^{59} is independently selected at each occurrence from C_{1-20} alkyl, C_{2-20} alkenyl, C_{2-20} alkynyl, 1- to 6-membered heteroalkyl, C_{3-12} carbocycle, and 3- to 12-membered heterocycle, each of which is optionally substituted by halogen, $-CN$, $-NO_2$, $-NH_2$, $-NHCH_3$, $-NHCH_2CH_3$, $=O$, $-OH$, $-OCH_3$, $-OCH_2CH_3$, C_{3-12} carbocycle, or 3- to 6-membered heterocycle.

12. The compound of claim 11, wherein the compound is a stereoisomer provided in at least 90% enantiomeric excess.

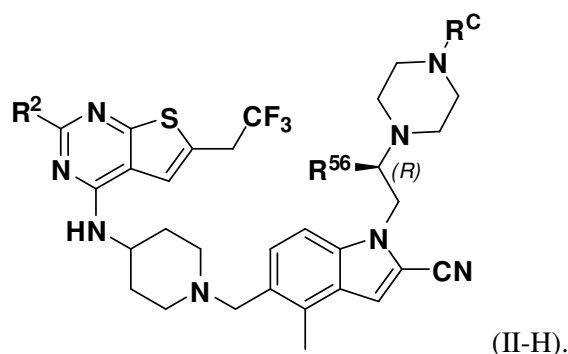
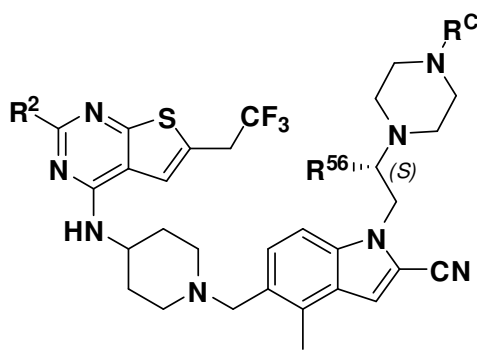
13. A pharmaceutical composition comprising a compound of any one of the preceding claims and a pharmaceutically acceptable carrier.

14. Use of a compound or salt of any one of claims 1 to 12 in the manufacture of a medicament for the treatment of leukemia, a hematologic malignancy, a solid tumor cancer, prostate cancer, breast cancer, liver cancer, a brain tumor, or diabetes.

15. The compound of claim 1, wherein the compound has the structure of Formula (II-C):



16. The compound of claim 1, wherein the compound has the structure of Formula (II-F) or Formula (II-H):



17. The compound of claim 1, wherein the compound is selected from the group consisting of:

