WHAT IS CLAIMED IS:

1. A method of identifying a subject having a hematological cancer who is likely to be responsive to a treatment compound or predicting the responsiveness of a subject having or suspected of having a hematological cancer to a treatment compound, comprising:

(a) obtaining a sample from the subject;

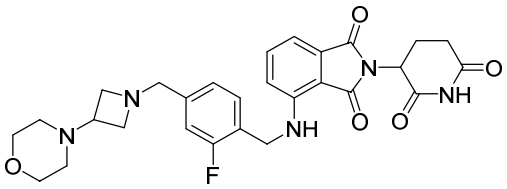
(b) determining a biomarker level in the sample;

(c) diagnosing the subject as being likely to be responsive to the treatment compound if:

(i) the biomarker level in the sample is detectable; or

(ii) the biomarker level in the sample is an altered level relative to a reference biomarker level; and

wherein the treatment compound is a compound of Formula (I):



(I),

or an enantiomer, mixture of enantiomers, tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

2. Use of a treatment compound in the manufacture of a medicament for~~A method of~~ selectively treating a hematological cancer in a subject having a hematological cancer, ~~comprising~~wherein:

(a) ~~obtaining~~ a sample from the subject having a hematological cancer is to be obtained;

(b) ~~determining~~ a biomarker level in the sample is to be determined;

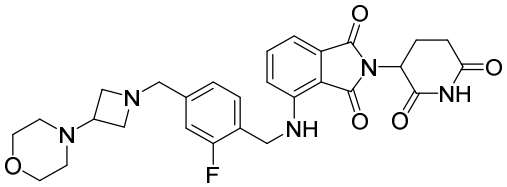
(c) ~~diagnosing~~ the subject is to be diagnosed as being likely to be responsive to the~~a~~ treatment compound if:

(i) the biomarker level in the sample is detectable; or

(ii) the biomarker level is an altered level relative to a reference level of the biomarker; and

(d) ~~administering~~ a therapeutically effective amount of the treatment compound is to be administered to the subject diagnosed as being likely to be responsive to the treatment compound;

wherein the treatment compound is a compound of Formula (I):



(I),

or an enantiomer, mixture of enantiomers, tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

3. The method of claim 1 or the use of claim 2, wherein the biomarker is cereblon (CRBN), and wherein ~~the method comprises diagnosing~~ the subject is to be diagnosed as being likely to be responsive to the treatment compound if CRBN is detectable or higher than a reference level in the sample.

4. The method of claim 1 or the use of claim 2, wherein the biomarker is Ikaros, Aiolos, ZFP91, or a combination thereof, and ~~wherein the method comprises diagnosing~~ the subject is to be diagnosed as being likely to be responsive to the treatment compound if the level of biomarker in the sample is lower than a reference level.

5. The method or use of claim 4, wherein the biomarker is the combination of Ikaros and Aiolos, and ~~wherein the method comprises diagnosing~~ the subject is to be diagnosed as being likely to be responsive to the treatment compound if the level of both Ikaros and Aiolos are lower than their respective reference levels.

6. A method of identifying a subject having a hematological cancer who is likely to be responsive to a treatment compound or predicting the responsiveness of a subject having or suspected of having a hematological cancer to a treatment compound, comprising:

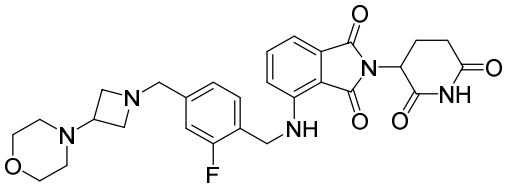
(a) obtaining a sample from the subject;

(b) administering the treatment compound to the sample;

(c) determining a biomarker level in the sample; and

(d) diagnosing the subject as being likely to be responsive to the treatment compound if the biomarker level in the sample is an altered level relative to a reference biomarker level;

wherein the treatment compound is a compound of Formula (I):



(I),

or an enantiomer, mixture of enantiomers, tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

7. A method of identifying a subject having a hematological cancer who is likely to be responsive to a treatment compound or predicting the responsiveness of a subject having or suspected of having a hematological cancer to a treatment compound, comprising:

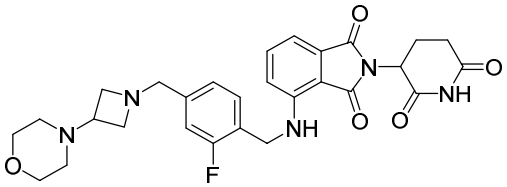
(a) ~~administering a treatment compound to a subject;~~

~~(b)~~ obtaining a sample from the subject who has been administered a treatment compound;

(~~c~~b) determining a biomarker level in the sample; and

(~~d~~c) diagnosing the subject as being likely to be responsive to the treatment compound if the biomarker level in the sample is an altered level relative to a reference biomarker level;

wherein the treatment compound is a compound of Formula (I):



(I),

or an enantiomer, mixture of enantiomers, tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

8. A method of monitoring the efficacy of a treatment compound in treating a hematological cancer in a subject, comprising:

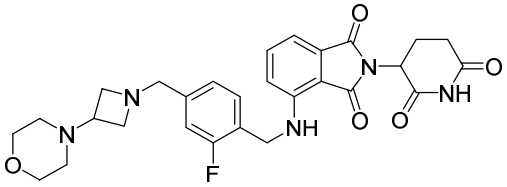
~~(a) administering a treatment compound to a subject;~~

(~~b~~a) obtaining a sample from the subject who has been administered a treatment compound;

(~~c~~b) determining a biomarker level in the sample; and

(~~d~~c) comparing the biomarker level in the sample with a reference biomarker level, wherein an altered biomarker level is indicative of the efficacy of the treatment compound in treating a hematological cancer in the subject;

wherein the treatment compound is a compound of Formula (I):



(I),

or an enantiomer, mixture of enantiomers, tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

9. A method of adjusting a dosage amount or frequency for treating a subject having a hematological cancer with a treatment compound comprising:

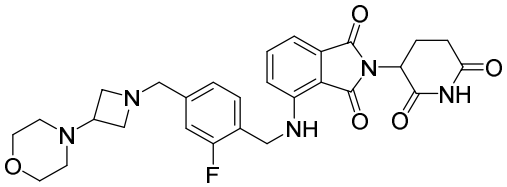
~~(a) administering a dosage of a treatment compound to a subject;~~

(~~b~~a) obtaining, at different time points, one of more samples from the subject who has been administered a dosage of a treatment compound~~at different time points~~; and

(~~c~~b) monitoring a biomarker level in the one or more samples, and

(~~d~~c) adjusting the dosage for subsequent administration of the treatment compound to the subject based upon an altered level of the biomarker in a reference sample,

wherein the treatment compound is a compound of Formula (I):



(I),

or an enantiomer, mixture of enantiomers, tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

10. The method of any one of claims 6 to 9, wherein ~~further comprising administering~~ a therapeutically effective amount of the treatment compound is to be administered to the subject diagnosed as being likely to be responsive to the treatment compound.

11. The method or use of any one of claims 1, 2, and 6 to 10, wherein the altered level of the biomarker in the sample is higher than the reference level of the biomarker.

12. The method or use of any one of claims 1, 2, and 6 to 10, wherein the altered level of the biomarker in the sample is lower than the reference level of the biomarker.

13. The method or use of any one of claims 1, 2, and 6 to 10, wherein an increased biomarker level relative to the reference biomarker level is indicative of the efficacy of the treatment compound in treating the hematological cancer in the subject.

14. The method or use of any one of claims 1, 2, and 6 to 10, wherein a decreased biomarker level relative to the reference biomarker level is indicative of the efficacy of the treatment compound in treating the hematological cancer in the subject.

15. The method or use of any one of claims 1, 2, and 6 to 10, wherein the reference biomarker level is the biomarker level in a reference sample obtained from the subject prior to ~~administering~~ administration of the treatment compound to the subject, and wherein the reference sample is from the same source as the sample.

16. The method or use of any one of claims 1, 2, and 6 to 10, wherein the reference biomarker level is the biomarker level in a reference sample obtained from a healthy subject not having the hematological cancer, and wherein the reference sample is from the same source as the sample.

17. The method or use of any one of claims 1, 2, and 6 to 10, wherein the reference biomarker level is a pre-determined biomarker level.

18. The method of any one of claims 6 to 10, wherein the biomarker comprises a marker of apoptosis, and wherein the alteration of the biomarker level is indicative of the induction of apoptosis.

19. The method of claim 18, wherein the biomarker is selected from the group consisting of cleaved caspase 3, cleaved caspase 7, cleaved poly (ADP-ribose) polymerase (PARP), BCL2, survivin, phosphatidylserine (PS) and DNA, Bcl-2-like protein 11 (BIM), tumor necrosis factor (TNF), interleukin-10 (IL-10), and interleukin-27 (IL27), or a combination thereof.

20. The method of claim 19, wherein the biomarker in the sample is higher than the reference level of the biomarker.

21. The method of claim 19, wherein the biomarker in the sample is lower than the reference level of the biomarker.

22. The method of claim 18, wherein the biomarker is selected from the group consisting of Annexin-V, 7-amino-actinomycin D (7-AAD), and Deep Red Anthraquinone 7 (DRAQ7), or a combination thereof.

23. The method of claim 22, wherein the biomarker in the sample is higher than the reference level of the biomarker.

24. The method of claim 22, wherein the biomarker in the sample is lower than the reference level of the biomarker.

25. The method of any one of claims 6 to 10, wherein the biomarker is selected from a group consisting of IL-8, IL-1a, sPGE2, sTNFα, sIgG, sIL-17A, sIL-17F, sIL-2, sIL-6, collagen-I and -III, PAI-1, CD69, and sIL-10, or a combination thereof.

26. The method of claim 25, wherein the biomarker in the sample is higher than the reference level of the biomarker.

27. The method of claim 25, wherein the biomarker in the sample is lower than the reference level of the biomarker.

28. The method of any one of claims 6 to 10, wherein the biomarker is associated with interferon signaling.

29. The method of claim 28, wherein the biomarker comprises interleukin-6 signal transducer (IL6ST), interferon-induced transmembrane protein 3 (IFITM3), interferon alpha-inducible protein 6 (IFI6), 2'-5'-oligoadenylate synthase 3 (OAS3), interferon α (IFNα), interferon β (IFN β), or a combination thereof.

30. The method of claim 28 or 29, wherein the biomarker in the sample is higher than the reference level of the biomarker.

31. The method of claim 28 or 29, wherein the biomarker in the sample is lower than the reference level of the biomarker.

32. The method of any one of claims 6 to 10, wherein the biomarker is associated with cytokine/chemokine signaling.

33. The method of claim 32, wherein the biomarker comprises interleukin-23 subunit alpha (IL23A), C-C motif chemokine 1 (CCL1), or a combination thereof.

34. The method of claim 32 or 33, wherein the biomarker in the sample is higher than the reference level of the biomarker.

35. The method of claim 32 or 33, wherein the biomarker in the sample is lower than the reference level of the biomarker.

36. The method of any one of claims 6 to 10, wherein the biomarker is associated with cell adhesion.

37. The method of claim 36, wherein the biomarker comprises E-selectin (SELE), P-selectin glycoprotein ligand 1 (SELPLG), thromboxane A2 (TXA2), or a combination thereof.

38. The method of claim 36 or 37, wherein the biomarker in the sample is higher than the reference level of the biomarker.

39. The method of claim 36 or 37, wherein the biomarker in the sample is lower than the reference level of the biomarker.

40. The method of any one of claims 6 to 10, wherein the biomarker is associated with cell-cell junction.

41. The method of claim 40, wherein the biomarker comprises claudin 7 (CLDN7), claudin 12 (CLDN12), or a combination thereof.

42. The method of claims 40 or 41, wherein the biomarker in the sample is higher than the reference level of the biomarker.

43. The method of claims 40 or 41, wherein the biomarker in the sample is lower than the reference level of the biomarker.

44. The method of any one of claims 6 to 10, wherein the biomarker is a G-protein coupled receptor.

45. The method of claim 44, wherein the biomarker comprises free fatty acid receptor 2 (FFAR2).

46. The method of claims 44 or 45, wherein the biomarker in the sample is higher than the reference level of the biomarker.

47. The method of claims 44 or 45, wherein the biomarker in the sample is lower than the reference level of the biomarker.

48. The method of any one of claims 6 to 10, wherein the biomarker is associated with extracellular matrix.

49. The method of claim 48, wherein the biomarker comprises CD209, SERPINA, SERPINB7, or a combination thereof.

50. The method of claim 48 or 49, wherein the biomarker in the sample is higher than the reference level of the biomarker.

51. The method of claim 48 or 49, wherein the biomarker in the sample is lower than the reference level of the biomarker.

52. The method of any one of claims 6 to 10, wherein the biomarker is associated with cell cycle.

53. The method of claim 52, wherein the biomarker in the sample is higher than the reference level of the biomarker.

54. The method of claim 52, wherein the biomarker in the sample is lower than the reference level of the biomarker.

55. The method of any one of claims 6 to 10, wherein the biomarker is associated with transcription.

56. The method of claim 55, wherein the biomarker in the sample is higher than the reference level of the biomarker.

57. The method of claim 55, wherein the biomarker in the sample is lower than the reference level of the biomarker.

58. The method of any one of claims 6 to 10, wherein the biomarker comprises one or more proteins selected from the group consisting of Aiolos (IKZF3), Ikaros (IKZF1), E3 ubiquitin-protein ligase ZFP91 (ZFP91), Protein C-ets-1 (ETS1), Max-binding protein MNT (MNT), myocyte-specific enhancer factor 2B (MEF2B), snRNA-activating protein complex subunit 1 (SNAPC1), lysine-specific demethylase 4B (KDM4B), transcription factor AP-4 (TFAP4), nucleolar transcription factor 1 (UBTF), bromo adjacent homology domain-containing 1 protein (BAHD1), methyl-CpG-binding domain protein 4 (MBD4), chromobox protein homolog 2 (CBX2), tumor protein 63 (TP63), transducin-like enhancer protein 3 (TLE3), forkhead box protein P1 (FOXP1), zinc finger and BTB domain-containing protein 11 (ZBTB11), interferon regulatory factor 4 (IRF4), mediator of RNA polymerase II transcription subunit 26 (MED26), cyclic AMP-dependent transcription factor ATF-7 (ATF7), zinc finger protein 644 (ZNF644), lysine-specific demethylase 5B (KDM5B), upstream stimulatory factor 2 (USF2), transcription factor 25 (TCF25), lysine-specific demethylase 4A (KDM4A), lethal (3) malignant brain tumor-like protein 2 (L3MBTL2), nRNA-activating protein complex subunit 4 (SNAPC4), lysine-specific demethylase 5 (KDM5), transcription factor COE1 (EBF1), forkhead box protein J2 (FOXJ2), nuclear factor of activated T-cells, cytoplasmic 1 (NFATC1), mRNA decay activator

protein ZFP36 (ZFP36), hepatoma-derived growth factor (HDGF), ETS-related transcription factor Elf-1 (ELF1), promyelocytic leukemia protein (PML), Myb-related protein B MYBL2, mothers against decapentaplegic homolog 2 (SMAD2), chromodomain-helicase-DNA-binding protein 2 (CHD2), signal transducer and activator of transcription 1 (STAT1), Paired box protein Pax-5 (PAX5), Signal transducer and activator of transcription 2 (STAT2), pygopus homolog 2 (PYGO2), interferon regulatory factor 9 (IRF9), polycomb group RING finger protein 2 (PCGF2), and cyclic AMP-dependent transcription factor ATF-3 (ATF3).

59. The method of claim 58, wherein the biomarker in the sample is higher than the reference level of the biomarker.

60. The method of claim 58, wherein the biomarker in the sample is lower than the reference level of the biomarker.

61. The method of any one of claims 6 to 10, wherein the biomarker comprises one or more genes selected from the group consisting of Interleukin-23 subunit alpha (IL23A), C-C motif chemokine 2 (CCL2), and SLIT-ROBO Rho GTPase-activating protein 1 (SRGAP1).

62. The method of claim 61, wherein the biomarker in the sample is higher than the reference level of the biomarker.

63. The method of claim 61, wherein the biomarker in the sample is lower than the reference level of the biomarker.

64. The method of any one of claims 6 to 10, wherein the biomarker comprises a CRBN-associated protein or a transcriptional target of a CRBN-associated protein.

65. The method of claim 64, wherein the CRBN-associated protein is selected from the group consisting of IKAROS, AIOLOS, and ZFP91.

66. The method of claim 64, wherein the transcriptional target of a CRBN-associated protein is selected from the group consisting of BCL6, c-MYC, and IRF4.

67. The method of claim 65 or 66, wherein the biomarker in the sample is higher than the reference level of the biomarker.

68. The method of claim 65 or 66, wherein the biomarker in the sample is lower than the reference level of the biomarker.

69. The method of claim 64, wherein the biomarker comprises an interferon inducible gene.

70. The method of claim 69, wherein the biomarker is selected from the group consisting of interferon regulatory 7 (IRF7), interferon induced protein with tetratricopeptide repeats 3 (IFIT3), DEAD box protein 58 (DDX58), and a combination thereof.

71. The method of claim 69 or 70, wherein the biomarker in the sample is higher than the reference level of the biomarker.

72. The method of claim 69 or 70, wherein the biomarker in the sample is lower than the reference level of the biomarker.

73. The method of claim 64, wherein the biomarker is selected from the group consisting of cyclin dependent kinase inhibitor 1 (p21).

74. The method of claim 73, wherein the biomarker in the sample is higher than the reference level of the biomarker.

75. The method of claim 73, wherein the biomarker in the sample is lower than the reference level of the biomarker.

76. The method of any one of claims 6 to 10, wherein the biomarker comprises a marker of T-cell activation.

77. The method of claim 76, wherein the marker of T-cell activation comprises a T-cell activation associated cytokine.

78. The method of claim 77, wherein the T-cell activation associated cytokine comprises interleukin 2 (IL-2).

79. The method of any one of claims 76 to 78, wherein the biomarker in the sample is higher than the reference level of the biomarker.

80. The method of any one of claims 76 to 78, wherein the biomarker in the sample is lower than the reference level of the biomarker.

81. The method of any one of claims 6 to 10, wherein the biomarker comprises PD1 and LAG3.

82. The method of claim 81, wherein the biomarker in the sample is higher than the reference level of the biomarker.

83. The method of claim 81, wherein the biomarker in the sample is lower than the reference level of the biomarker.

84. The method of any one of claims 6 to 10, wherein the biomarker comprises an effector cytokine or effector chemokine.

85. The method of claim 84, wherein the biomarker is selected from the group consisting of granulocyte-macrophage colony-stimulating factor (GM-CSF), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and a combination thereof.

86. The method of claim 84 or 85, wherein the biomarker in the sample is higher than the reference level of the biomarker.

87. The method of claim 84 or 85, wherein the biomarker in the sample is lower than the reference level of the biomarker.

88. The method or use of any one of claims 1 to 87, wherein the biomarker is expressed in a white blood cell.

89. The method or use of claim 88, wherein the white blood cell comprises a lymphoid cell.

90. The method or use of claim 89, wherein the lymphoid cell comprises a T-cell.

91. ~~A method~~Use of a treatment compound in the manufacture of a medicament for treating a hematological cancer, ~~comprising~~wherein:

(a) ~~obtaining~~ a first sample is to be obtained from a subject having a hematological cancer;

(b) ~~determining~~ a biomarker level in the first sample is to be determined;

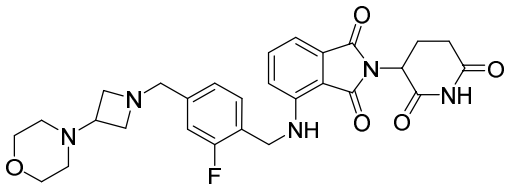
(c) ~~administering~~ a therapeutically effective amount of the~~a~~ treatment compound is to be administered to the subject;

(d) ~~obtaining~~ at least one additional sample is to be obtained from the subject after the treatment; and

(e) ~~determining~~ the biomarker level in the at least one additional sample is to be determined; and

if the biomarker level in the at least one additional sample is at or near the biomarker level of the first sample, then ~~administering~~ another therapeutically effective amount of the treatment compound is to be administered to the subject,

wherein the treatment compound is a compound of Formula (I):



(I),

or an enantiomer, mixture of enantiomers, tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

92. The ~~method~~use of claim 91, wherein the biomarker comprises Ikaros.

93. The ~~method~~use of claim 92, wherein the biomarker is expressed in a white blood cell.

94. The ~~method~~use of claim 93, wherein the white blood cell comprises a myeloid cell.

95. The ~~method~~use of claim 94, wherein the myeloid cell comprises a neutrophil.

96. The ~~method~~use of claim 91, wherein the biomarker comprises neutrophils having a phenotype of $CD11b^+$, $CD34^-$, and $CD33^-$.

97. The method or use of any one of claims 1 to 96, wherein the compound comprises (S)-2-(2,6-Dioxopiperidin-3-yl)-4-((2-fluoro-4-((3-morpholinoazetidin-1-yl)methyl)benzyl)amino)isoindoline-1,3-dione, or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

98. The method or use of any one of claims 1 to 96, wherein the compound comprises (R)-2-(2,6-Dioxopiperidin-3-yl)-4-((2-fluoro-4-((3-morpholinoazetidin-1-yl)methyl)benzyl)amino)isoindoline-1,3-dione, or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

99. The method or use of any one of claims 1 to 96, wherein the compound comprises a mixture of (S)-2-(2,6-Dioxopiperidin-3-yl)-4-((2-fluoro-4-((3-morpholinoazetidin-1-yl)methyl)benzyl)amino)isoindoline-1,3-dione, and (R)-2-(2,6-Dioxopiperidin-3-yl)-4-((2-fluoro-4-((3-morpholinoazetidin-1-yl)methyl)benzyl)amino)isoindoline-1,3-dione, or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof.

100. The method or use of any one of claims 1 to 99, ~~further comprising administering~~ a therapeutically effective amount of a second active agent or a support care therapy is to be administered.

101. The method or use of claim 100, wherein the second active agent is selected from the group consisting of an HDAC inhibitor (*e.g.*, panobinostat, romidepsin, vorinostat, or citarinostat), a BCL2 inhibitor (*e.g.*, venetoclax), a BTK inhibitor (*e.g.*, ibrutinib or acalabrutinib), an mTOR inhibitor (*e.g.*, everolimus), a PI3K inhibitor (*e.g.*, idelalisib), a PKCβ inhibitor (*e.g.*, enzastaurin), a SYK inhibitor (*e.g.*, fostamatinib), a JAK2 inhibitor (*e.g.*, fedratinib, pacritinib, ruxolitinib, baricitinib, gandotinib, lestaurtinib, or momelotinib), an Aurora A kinase inhibitor (*e.g.*, alisertib), an EZH2 inhibitor (*e.g.*, tazemetostat, GSK126, CPI-1205, 3-deazaneplanocin A, EPZ005687, EI1, UNC1999, or sinefungin), a BET inhibitor (*e.g.*, birabresib or 4-[2-(cyclopropylmethoxy)-5-(methanesulfonyl)phenyl]-2-methylisoquinolin-1(2H)-one), a hypomethylating agent (*e.g.*, 5-azacytidine or decitabine), a chemotherapy (*e.g.*, bendamustine, doxorubicin, etoposide, methotrexate, cytarabine, vincristine, ifosfamide, melphalan, dexamethasone, or oxaliplatin), an anti-CD20 monoclonal antibody (*e.g.*, rituximab, or obinutuzumab), an epigenetic compound, or a combination thereof.

102. The method or use of claim 101, wherein the second active agent comprises rituximab.

103. The method or use of claim 101, wherein the second active agent comprises obinutuzumab.

104. The method or use of any one of claims 1 to 103, wherein the hematological cancer affects the hematopoietic or lymphoid tissues.

105. The method or use of any one of claims 1 to 104, wherein the hematological cancer comprises non-Hodgkin's lymphoma.

106. The method or use of claim 105, wherein the non-Hodgkin's lymphoma comprises diffuse large B-cell lymphoma (DLBCL).

107. The method or use of claim 106, wherein the DLBCL is relapsed, refractory, or resistant to conventional therapy.

108. The method or use of claim 104, wherein the hematological cancer comprises chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL).

109. The method or use of claim 108-, wherein the CLL/SLL is relapsed, refractory, or resistant to conventional therapy.

110. The method or use of any one of claims 1 to 109, wherein the sample comprises a hematological cancer cell.

111. The method or use of any one of claims 1 to 110, wherein determining the biomarker level comprises determining the protein level of the biomarker.

112. The method or use of any one of claims 1 to 110, wherein determining the biomarker level comprises determining the mRNA level of the biomarker.

113. The method or use of any one of claims 1 to 110, wherein determining the biomarker level comprises determining the cDNA level of the biomarker.