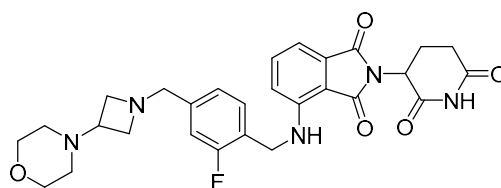


WHAT IS CLAIMED IS:

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) determining a biomarker level in a sample obtained from the subject;
 - (b) diagnosing the subject as being likely to be responsive to the treatment compound if the biomarker is cereblon (CRBN) and the level of CRBN in the sample is detectable; and
- wherein the treatment compound is a compound of Formula (I):

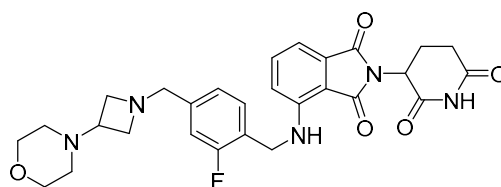


(I),

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 selectively treating a hematological cancer in a subject having a hematological cancer, wherein:
- (a) a sample from the subject having a hematological cancer is to be obtained;
 - (b) a biomarker level in the sample is to be determined;
 - (c) the subject is to be diagnosed as being likely to be responsive to the treatment compound if the biomarker is CRBN and the level of CRBN in the sample is detectable; and
 - (d) 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. 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 the treatment compound to a sample obtained from the subject;
- (b) determining a biomarker level in the sample; and
- (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 biomarker comprises one or more of:

(A) an apoptotic marker selected from the group consisting of IL27, TNF, IL10, cleaved caspase 3, cleaved caspase 7, and cleaved poly (ADP-ribose) polymerase (PARP);

(B) sIL-2 and sIL-6;

(C) an interferon signaling associated marker selected from the group consisting of 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 (IFN α), and interferon β (IFN β);

(D) a cytokine/chemokine signaling associated marker 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);

(E) a cell adhesion associated marker selected from the group consisting of E-selectin (SELE), P-selectin glycoprotein ligand 1 (SELPLG), and thromboxane A2 (TXA2);

(F) a cell-cell junction associated marker selected from the group consisting of claudin 7 (CLDN7), and claudin 12 (CLDN12);

(G) free fatty acid receptor 2 (FFAR2);

(H) an extracellular matrix associated marker selected from the group consisting of CD209, SERPINA, and SERPINB7;

(I) an interferon inducible gene selected from the group consisting of interferon regulatory 7 (IRF7), interferon induced protein with tetratricopeptide repeats 3 (IFIT3), and DEAD box protein 58 (DDX58);

(J) cyclin dependent kinase inhibitor 1 (p21);

(K) PD1 and LAG3;

(L) an effector cytokine or effector chemokine selected from the group consisting of granulocyte-macrophage colony-stimulating factor (GM-CSF), tumor necrosis factor alpha (TNF α), and interferon gamma (IFN γ);

(M) a CRBN-associated protein selected from the group consisting of Ikaros, Aiolos, and ZFP91;

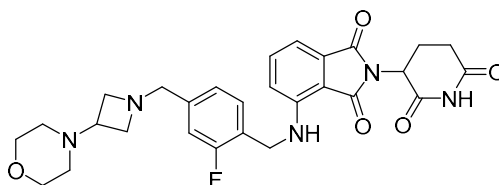
(N) a transcriptional target of a CRBN-associated protein selected from the group consisting of c-MYC, IRF4, and BCL6;

(O) BCL2 and survivin;

(P) IL-8, IL-1a, sPGE2, sTNF α , sIgG, sIL-17A, sIL-17F, collagen-I and -III, and PAI-1; or

(Q) a T-cell activation associated cytokine;

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



(I),

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

4. 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:

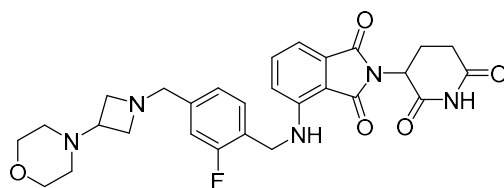
(a) determining a biomarker level in a sample obtained from the subject who has been administered a treatment compound; and

(b) 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 biomarker comprises one or more of:

- (A) an apoptotic marker selected from the group consisting of IL27, TNF, IL10, cleaved caspase 3, cleaved caspase 7, and PARP;
- (B) sIL-2 and sIL-6;
- (C) an interferon signaling associated marker selected from the group consisting of IL6ST, IFITM3, IFI6, OAS3, IFN α , and IFN β ;
- (D) a cytokine/chemokine signaling associated marker selected from the group consisting of IL23A, CCL2, and SRGAP1;
- (E) a cell adhesion associated marker selected from the group consisting of SELE, SELPLG, and TXA2;
- (F) a cell-cell junction associated marker selected from the group consisting of CLDN7, and CLDN12;
- (G) FFAR2;
- (H) an extracellular matrix associated marker selected from the group consisting of CD209, SERPINA, and SERPINB7;
- (I) an interferon inducible gene selected from the group consisting of IRF7, IFIT3, and DDX58;
- (J) p21;
- (K) PD1 and LAG3;
- (L) an effector cytokine or effector chemokine selected from the group consisting of GM-CSF, TNF α , and IFN γ ;
- (M) a CRBN-associated protein selected from the group consisting of Ikaros, Aiolos, and ZFP91;
- (N) a transcriptional target of a CRBN-associated protein selected from the group consisting of c-MYC, IRF4, and BCL6;
- (O) BCL2 and survivin;
- (P) IL-8, IL-1 α , sPGE2, sTNF α , sIgG, sIL-17A, sIL-17F, collagen-I and -III, and PAI-1; or
- (Q) a T-cell activation associated cytokine;

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



(I),

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

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

(a) determining a biomarker level in a sample obtained from the subject who has been administered a treatment compound; and

(b) 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 biomarker comprises one or more of:

(A) an apoptotic marker selected from the group consisting of IL27, TNF, IL10, cleaved caspase 3, cleaved caspase 7, and PARP;

(B) sIL-2 and sIL-6;

(C) an interferon signaling associated marker selected from the group consisting of IL6ST, IFITM3, IFI6, OAS3, IFN α , and IFN β ;

(D) a cytokine/chemokine signaling associated marker selected from the group consisting of IL23A, CCL2, and SRGAP1;

(E) a cell adhesion associated marker selected from the group consisting of SELE, SELPLG, and TXA2;

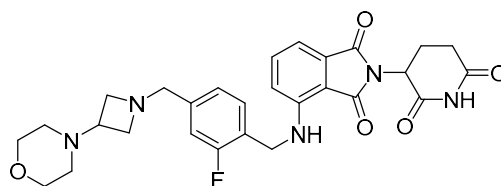
(F) a cell-cell junction associated marker selected from the group consisting of CLDN7, and CLDN12;

(G) FFAR2;

(H) an extracellular matrix associated marker selected from the group consisting of CD209, SERPINA, and SERPINB7;

(I) an interferon inducible gene selected from the group consisting of IRF7, IFIT3, and DDX58;

- (J) p21;
 - (K) PD1 and LAG3;
 - (L) an effector cytokine or effector chemokine selected from the group consisting of GM-CSF, TNF α , and IFN γ ;
 - (M) a CRBN-associated protein selected from the group consisting of Ikaros, Aiolos, and ZFP91;
 - (N) a transcriptional target of a CRBN-associated protein selected from the group consisting of c-MYC, IRF4, and BCL6;
 - (O) BCL2 and survivin;
 - (P) IL-8, IL-1 α , sPGE2, sTNF α , sIgG, sIL-17A, sIL-17F, collagen-I and -III, and PAI-1; or
 - (Q) a T-cell activation associated cytokine;
- wherein the treatment compound is a compound of Formula (I):



(I),

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

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

- (a) monitoring a biomarker level in one or more samples obtained, at different time points, from the subject who has been administered a dosage of a treatment compound, and
- (b) adjusting the dosage of the treatment compound to be subsequently administered to the subject based upon an altered level of the biomarker in a reference sample;

wherein the biomarker comprises one or more of:

- (A) an apoptotic marker selected from the group consisting of IL27, TNF, IL10, cleaved caspase 3, cleaved caspase 7, and PARP;
- (B) sIL-2 and sIL-6;

(C) an interferon signaling associated marker selected from the group consisting of IL6ST, IFITM3, IFI6, OAS3, IFN α , and IFN β ;

(D) a cytokine/chemokine signaling associated marker selected from the group consisting of IL23A, CCL2, and SRGAP1;

(E) a cell adhesion associated marker selected from the group consisting of SELE, SELPLG, and TXA2;

(F) a cell-cell junction associated marker selected from the group consisting of CLDN7, and CLDN12;

(G) FFAR2;

(H) an extracellular matrix associated marker selected from the group consisting of CD209, SERPINA, and SERPINB7;

(I) an interferon inducible gene selected from the group consisting of IRF7, IFIT3, and DDX58;

(J) p21;

(K) PD1 and LAG3;

(L) an effector cytokine or effector chemokine selected from the group consisting of GM-CSF, TNF α , and IFN γ ;

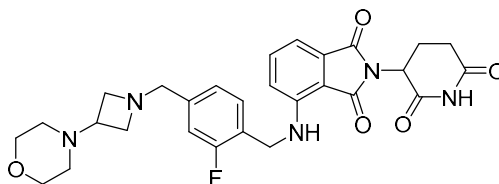
(M) a CRBN-associated protein selected from the group consisting of Ikaros, Aiolos, and ZFP91;

(N) a transcriptional target of a CRBN-associated protein selected from the group consisting of c-MYC, IRF4, and BCL6;

(O) BCL2 and survivin;

(P) IL-8, IL-1 α , sPGE2, sTNF α , sIgG, sIL-17A, sIL-17F, collagen-I and -III, and PAI-1; or

(Q) a T-cell activation associated cytokine; 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. The method of any one of claims 3 to 6, wherein 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.

8. The method or use of any one of claims 1 to 7, wherein the reference biomarker level is the biomarker level in a reference sample obtained from the subject prior to administration of the treatment compound to the subject, and wherein the reference sample is from the same source as the sample.

9. The method or use of any one of claims 1 to 7, 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.

10. The method or use of any one of claims 1 to 7, wherein the reference biomarker level is a pre-determined biomarker level.

11. The method of any one of claims 3 to 7, wherein the biomarker comprises a marker of apoptosis, and wherein the alteration of the biomarker level is indicative of the induction of apoptosis.

12. The method of claim 11, wherein the biomarker is selected from the group consisting of cleaved caspase 3, cleaved caspase 7, cleaved poly PARP, TNF, IL-10, and IL27, or a combination thereof.

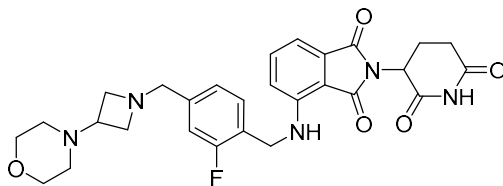
13. The method of claim 11, wherein the biomarker is selected from the group consisting of BCL2, and survivin, or a combination thereof.

14. The method of any one of claims 3 to 7, wherein the biomarker is selected from the group consisting of IL-8, IL-1a, sPGE2, sTNF α , sIgG, sIL-17A, sIL-17F, collagen-I and -III, and PAI-1, or a combination thereof.

15. The method of any one of claims 3 to 7, wherein the biomarker is selected from the group consisting of sIL-2, and sIL-6, or a combination thereof.
16. The method of any one of claims 3 to 7, wherein the biomarker is associated with interferon signaling.
17. The method of claim 16, wherein the biomarker is selected from the group consisting of IL6ST, IFITM3, IFI6, OAS3, IFN α , and IFN β , or a combination thereof.
18. The method of any one of claims 3 to 7, wherein the biomarker is associated with cytokine/chemokine signaling.
19. The method of claim 18, wherein the biomarker is selected from the group consisting of IL23A, CCL2, and SRGAP1, or a combination thereof.
20. The method of any one of claims 3 to 7, wherein the biomarker is associated with cell adhesion.
21. The method of claim 20, wherein the biomarker is selected from the group consisting of SELE, SELPLG, and TXA2, or a combination thereof.
22. The method of any one of claims 3 to 7, wherein the biomarker is associated with cell-cell junction.
23. The method of claim 22, wherein the biomarker is selected from the group consisting of CLDN7, and CLDN12, or a combination thereof.
24. The method of any one of claims 3 to 7, wherein the biomarker is a G-protein coupled receptor.
25. The method of claim 24, wherein the biomarker comprises FFAR2.
26. The method of any one of claims 3 to 7, wherein the biomarker is associated with extracellular matrix.

27. The method of claim 26, wherein the biomarker is selected from the group consisting of CD209, SERPINA, and SERPINB7, or a combination thereof.
28. The method of any one of claims 3 to 7, wherein the biomarker comprises a CRBN-associated protein or a transcriptional target of a CRBN-associated protein.
29. The method of claim 28, wherein the CRBN-associated protein is selected from the group consisting of IKAROS, AIOLOS, and ZFP91, or a combination thereof.
30. The method of claim 28, wherein the transcriptional target of a CRBN-associated protein is selected from the group consisting of BCL6, c-MYC, and IRF4, or a combination thereof.
31. The method of any one of claims 3 to 7, wherein the biomarker comprises an interferon inducible gene.
32. The method of claim 31, wherein the biomarker is selected from the group consisting of IRF7, IFIT3, and DDX58, or a combination thereof.
33. The method of any one of claims 3 to 7, wherein the biomarker is selected from the group consisting of p21.
34. The method of any one of claims 3 to 7, wherein the biomarker comprises a marker of T-cell activation.
35. The method of claim 34, wherein the marker of T-cell activation comprises a T-cell activation associated cytokine.
36. The method of claim 35, wherein the T-cell activation associated cytokine comprises IL-2.
37. The method of any one of claims 3 to 7, wherein the biomarker comprises PD1 and LAG3.
38. The method of any one of claims 3 to 7, wherein the biomarker comprises an effector cytokine or effector chemokine.

39. The method of claim 38, wherein the biomarker is selected from the group consisting of GM-CSF, $\text{TNF}\alpha$, and $\text{IFN}\gamma$, or a combination thereof.
40. The method or use of any one of claims 1 to 39, wherein the biomarker is expressed in a white blood cell.
41. The method or use of claim 40, wherein the white blood cell comprises a lymphoid cell.
42. The method or use of claim 41, wherein the lymphoid cell comprises a T-cell.
43. The method of any one of claims 11, 12, 15 to 27, and 31 to 39, wherein the biomarker in the sample is higher than the reference level of the biomarker.
44. The method of any one of claims 13, 14, 28 to 30, wherein the biomarker in the sample is lower than the reference level of the biomarker.
45. Use of a treatment compound in the manufacture of a medicament for treating a hematological cancer, wherein:
- (a) a first sample is to be obtained from a subject having a hematological cancer;
 - (b) a biomarker level in the first sample is to be determined;
 - (c) a therapeutically effective amount of the treatment compound is to be administered to the subject;
 - (d) at least one additional sample is to be obtained from the subject after the treatment; and
 - (e) 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 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;

wherein the biomarker

(i) comprises Ikaros; or

(ii) comprises neutrophils having a phenotype of CD11b⁺, CD34⁺, and CD33⁺.

46. The use of claim 45, wherein the biomarker comprises Ikaros.

47. The use of claim 46, wherein the biomarker is expressed in a white blood cell.

48. The use of claim 47, wherein the white blood cell comprises a myeloid cell.

49. The use of claim 48, wherein the myeloid cell comprises a neutrophil.

50. The use of claim 45, wherein the biomarker comprises neutrophils having a phenotype of CD11b⁺, CD34⁺, and CD33⁺.

51. The method or use of any one of claims 1 to 50, 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.

52. The method or use of any one of claims 1 to 50, 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.

53. The method or use of any one of claims 1 to 50, 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.

54. The method or use of any one of claims 1 to 53, a therapeutically effective amount of a second active agent or a support care therapy is to be administered.
55. The method or use of claim 54, 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 PKC β 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.
56. The method or use of claim 55, wherein the second active agent comprises rituximab.
57. The method or use of claim 55, wherein the second active agent comprises obinutuzumab.
58. The method or use of any one of claims 1 to 57, wherein the hematological cancer affects the hematopoietic or lymphoid tissues.
59. The method or use of any one of claims 1 to 58, wherein the hematological cancer comprises non-Hodgkin's lymphoma.
60. The method or use of claim 59, wherein the non-Hodgkin's lymphoma comprises diffuse large B-cell lymphoma (DLBCL).
61. The method or use of claim 60, wherein the DLBCL is relapsed, refractory, or resistant to conventional therapy.

62. The method or use of claim 58, wherein the hematological cancer comprises chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL).
63. The method or use of claim 62, wherein the CLL/SLL is relapsed, refractory, or resistant to conventional therapy.
64. The method or use of any one of claims 1 to 63, wherein the sample comprises a hematological cancer cell.
65. The method or use of any one of claims 1 to 64, wherein determining the biomarker level comprises determining the protein level of the biomarker.
66. The method or use of any one of claims 1 to 64, wherein determining the biomarker level comprises determining the mRNA level of the biomarker.
67. The method or use of any one of claims 1 to 64, wherein determining the biomarker level comprises determining the cDNA level of the biomarker.