WHAT IS CLAIMED IS:

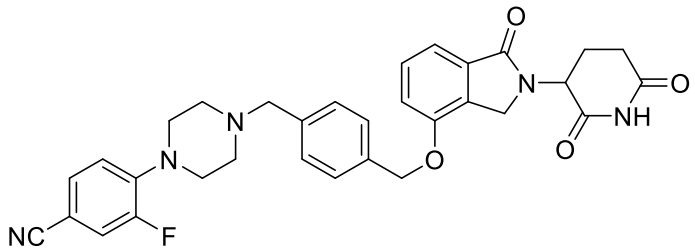
1. A method of identifying a subject having cancer who is likely to be responsive to a treatment compound, comprising:

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

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 1:



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

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

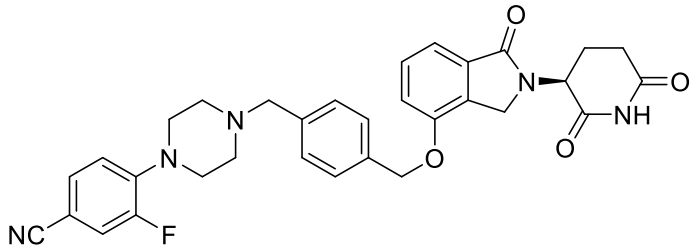
2. A method of identifying a subject having cancer who is likely to be responsive to a treatment compound, comprising:

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

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

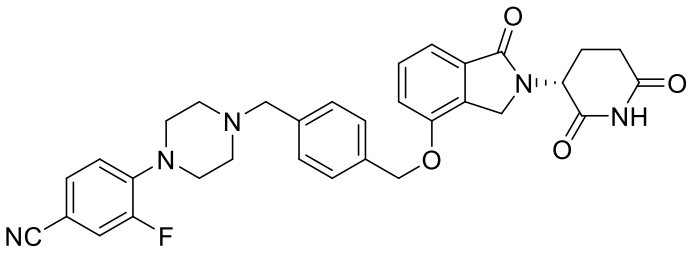
3. A method of identifying a subject having cancer who is likely to be responsive to a treatment compound, comprising:

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

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

4. A method of identifying a subject having cancer who is likely to be responsive to a treatment compound, comprising:

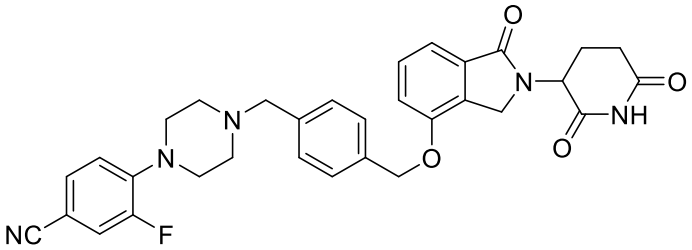
(a) obtaining a sample from the subject;

(b) administering the treatment compound to the sample;

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

(d) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 1:



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

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

5. A method of identifying a subject having cancer who is likely to be responsive to a treatment compound, comprising:

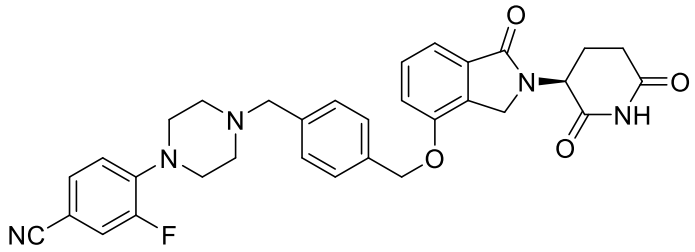
(a) obtaining a sample from the subject;

(b) administering the treatment compound to the sample;

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

(d) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

6. A method of identifying a subject having cancer who is likely to be responsive to a treatment compound, comprising:

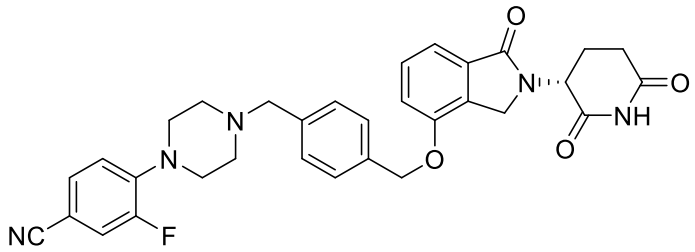
(a) obtaining a sample from the subject;

(b) administering the treatment compound to the sample;

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

(d) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

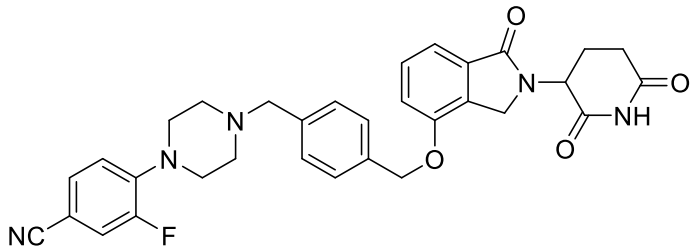
7. A method of predicting the responsiveness of a subject having or suspected of having cancer to a treatment compound, comprising:

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

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from the level of the biomarker obtained from a reference sample;

wherein the treatment compound is Compound 1:



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

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

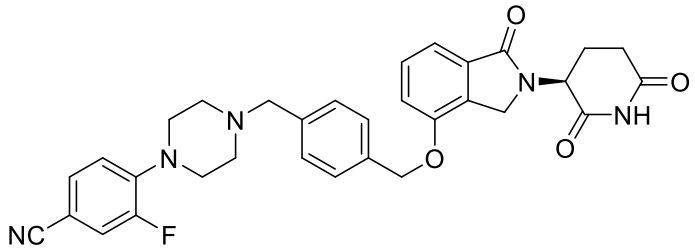
8. A method of predicting the responsiveness of a subject having or suspected of having cancer to a treatment compound, comprising:

(a) obtaining a sample from the subject;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from the level of the biomarker obtained from a reference sample;

wherein the treatment compound is Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

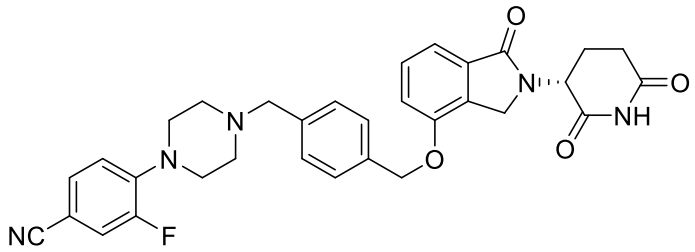
9. A method of predicting the responsiveness of a subject having or suspected of having cancer to a treatment compound, comprising:

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

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from the level of the biomarker obtained from a reference sample;

wherein the treatment compound is Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof , and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

10. A method of predicting the responsiveness of a subject having or suspected of having cancer to a treatment compound, comprising:

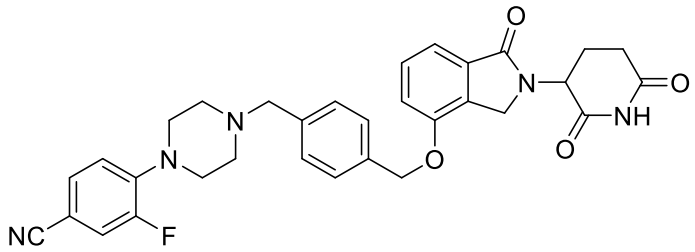
(a) obtaining a sample from the subject;

(b) administering the treatment compound to the sample;

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

(d) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from the level of the biomarker obtained from a reference sample;

wherein the treatment compound is Compound 1:



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

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

11. A method of predicting the responsiveness of a subject having or suspected of having cancer to a treatment compound, comprising:

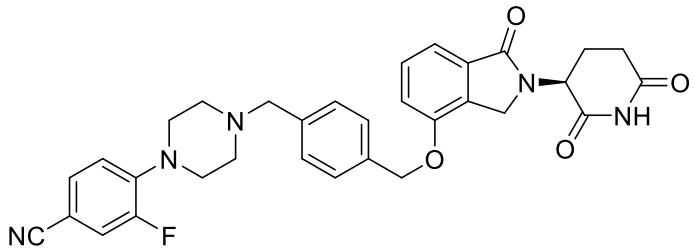
(a) obtaining a sample from the subject;

(b) administering the treatment compound to the sample;

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

(d) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from the level of the biomarker obtained from a reference sample;

wherein the treatment compound is Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

12. A method of predicting the responsiveness of a subject having or suspected of having cancer to a treatment compound, comprising:

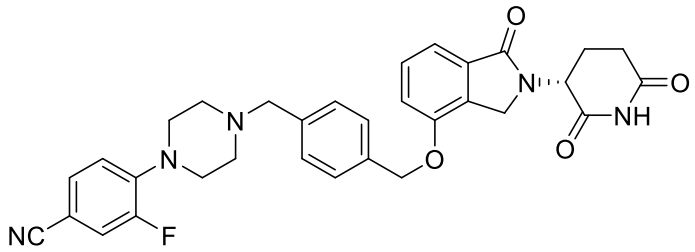
(a) obtaining a sample from the subject;

(b) administering the treatment compound to the sample;

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

(d) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from the level of the biomarker obtained from a reference sample;

wherein the treatment compound is Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

13. The method of any one of claims 1-12, wherein the level of the biomarker in the sample is higher than the reference level of the biomarker.

14. The method of any one of claims 1-12, wherein the level of the biomarker in the sample is lower than the reference level of the biomarker.

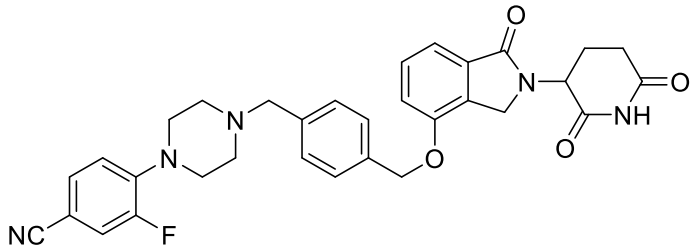
15. A method of monitoring the efficacy of a treatment compound in treating cancer in a subject, comprising:

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

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

(c) comparing the level of the biomarker in the sample with the level of the biomarker obtained from a reference sample, wherein a change in the biomarker level is indicative of the efficacy of the treatment compound in treating the cancer in the subject;

wherein the treatment compound is Compound 1:



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

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

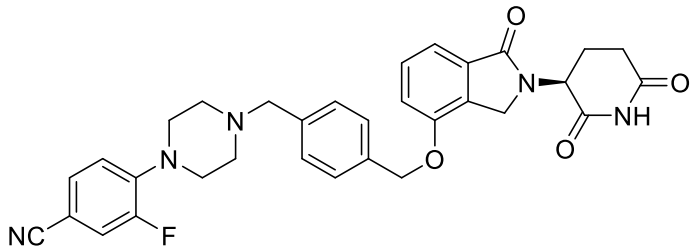
16. A method of monitoring the efficacy of a treatment compound in treating cancer in a subject, comprising:

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

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

(c) comparing the level of the biomarker in the sample with the level of the biomarker obtained from a reference sample, wherein a change in the biomarker level is indicative of the efficacy of the treatment compound in treating the cancer in the subject;

wherein the treatment compound is Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

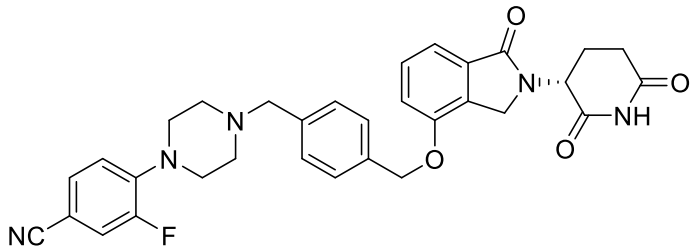
17. A method of monitoring the efficacy of a treatment compound in treating cancer in a subject, comprising:

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

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

(c) comparing the level of the biomarker in the sample with the level of the biomarker obtained from a reference sample, wherein a change in the biomarker level is indicative of the efficacy of the treatment compound in treating the cancer in the subject;

wherein the treatment compound is Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

18. The method of claims 15-17, wherein an increased level of the biomarker as compared to the reference level is indicative of the efficacy of the treatment compound in treating the cancer in the subject.

19. The method of claims 15-17, wherein a decreased level of the biomarker as compared to the reference level is indicative of the efficacy of the treatment compound in treating the cancer in the subject.

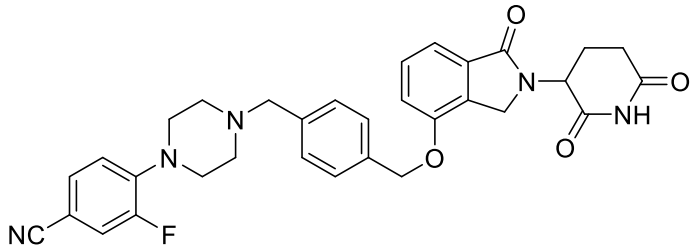
20. Use of a therapeutically effective amount of a treatment compound in the manufacture of a medicament for treating cancer in a subject, wherein the subject has been identified as being likely to be responsive to the treatment compound by a method comprising:

(a) obtaining a sample from the subject having the cancer;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 1:



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

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

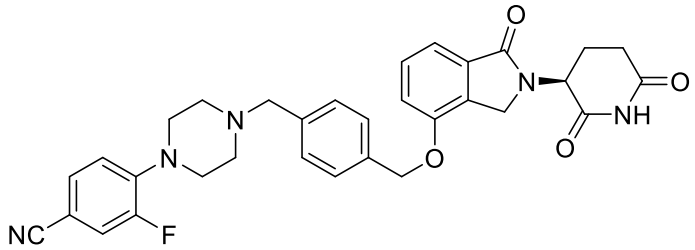
21. Use of a therapeutically effective amount of a treatment compound in the manufacture for a medicament for treating cancer in a subject, wherein the subject has been identified as being likely to be responsive to the treatment compound by a method comprising:

(a) obtaining a sample from the subject having the cancer;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

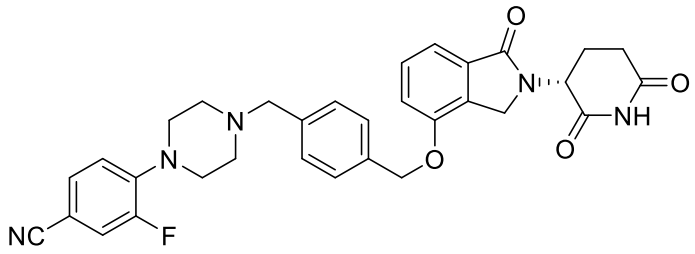
22. Use of a therapeutically effective amount of a treatment compound in the manufacture of a medicament for treating cancer in a subject, wherein the subject has been identified as being likely to be responsive to the treatment compound by a method comprising:

(a) obtaining a sample from the subject having the cancer;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is different from a reference level of the biomarker;

wherein the treatment compound is Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises one or more of the following:

(i) cereblon (CRBN);

(ii) a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4;

(iii) an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC);

(iv) a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl);

(v) a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality; and/or

(vi) circulating tumor cells (CTCs).

23. The use of any one of claims 20-22, wherein the level of the biomarker in the sample is higher than the reference level of the biomarker.

24. The use of any one of claims 20-22, wherein the level of the biomarker in the sample is lower than the reference level of the biomarker.

25. The use of any one of claims 20-24, wherein the 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.

26. The use of any one of claims 20-25, wherein a therapeutically effective amount of a second active agent or a support care therapy is to be further administered to the subject.

27. The use of claim 26, wherein the second active agent is selected from the group comprising large molecules, small molecules, or cell therapies, and the second active agent is optionally selected from a group comprising of melphalan, vincristine, cyclophosphamide, etoposide, doxorubicin, bendamustine, a proteasome inhibitor, a histone deacetylase inhibitor, a BET inhibitor, a BCL2 inhibitor, an MCL-1 inhibitor, a corticosteroid, dexamethasone, an antibody, a checkpoint inhibitor, and CAR cells.

28. The method of any one of claims 1-19, and the use of any one of claims 20-27, wherein the reference sample is obtained from the subject before the subject has been administered with the treatment compound, and wherein the reference sample is from the same source as the sample.

29. The method of any one of claims 1-19 and the use of any one of claims 20-27, wherein the reference sample is obtained from a healthy subject not having the cancer, and wherein the reference sample is from the same source as the sample.

30. The method of any one of claims 1-19 and the use of any one of claims 20-27, wherein the reference sample is obtained from a subject receiving an anti-cancer compound that is not said treatment compound, and wherein the reference sample is from the same source as the sample.

31. The method and the use of any one of claim 30, wherein said anti-cancer compound is lenalidomide, or pomalidomide.

32. The method of any one of claims 1-19 or 28-31 and the use of any one of claims 20-24 or 28-31, wherein the cancer is multiple myeloma (MM).

33. The method and the use of claim 32, wherein the MM is relapsed, refractory, or resistant to conventional therapy.

34. The method of any one of claims 1-19 or 28-33 and the use of any one of claims 20-24 or 28-33, wherein the biomarker is cereblon (CRBN).

35. The method of any one of claims 1-19 or 28-33 and the use of any one of claims 20-24 or 28-33, wherein the biomarker is a CRBN-associated protein selected from the group consisting of IKZF1, IKZF3, ZFP91, c-MYC, and IRF4.

36. The method of any one of claims 1-19 or 28-33 and the use of any one of claims 20-24 or 28-33, wherein the biomarker is an apoptotic marker selected from the group consisting of cleaved Caspase-l (c-Caspase-l), cleaved Caspase-3 (c-Caspase-3), cleaved Caspase-7 (c-Caspase-7), cleaved PARP, survivin, BIM BCL-2 like protein 11 (BIM), and serum free light chain (sFLC).

37. The method of any one of claims 1-19 or 28-33 and the use of any one of claims 20-24 or 28-33, wherein the biomarker is a marker of cell cycle arrest selected from the group consisting of: cyclin-dependent kinase inhibitor 1 (p2l), cyclin-dependent kinase inhibitor 1B (p27), and retinoblastoma protein (pRbl).

38. The method of any one of claims 1-19 or 28-33 and the use of any one of claims 20-24 or 28-33, wherein the biomarker is a marker of T-cell activation selected from the group consisting of soluble CD25 (sCD25), interleukin-2 (IL-2), tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and T-cell receptor (TCR) clonality.

39. The method of any one of claims 1-19 or 28-33 and the use of any one of claims 20-24 or 28-33, wherein the biomarker is circulating tumor cells (CTCs).

40. The method and the use of claim 35, wherein the biomarker is IKZF1.

41. The method and the use of claim 35, wherein the biomarker is IKZF3.

42. The method and the use of claim 35, wherein the biomarker is ZFP91.

43. The method and the use of claim 35, wherein the biomarker is c-MYC.

44. The method and the use of claim 35, wherein the biomarker is IRF4

45. The method and the use of claim 36, wherein the biomarker is cleaved Caspase-3 (c-Caspase-3).

46. The method and the use of claim 36, wherein the biomarker is cleaved Caspase-1 (c-Caspase-1).

47. The method and the use of claim 36, wherein the biomarker is cleaved Caspase-7 (c-Caspase-7).

48. The method and the use of claim 36, wherein the biomarker is cleaved PARP.

49. The method and the use of claim 36, wherein the biomarker is survivin.

50. The method and the use of claim 36, wherein the biomarker is BCL-2 like protein 11 (BIM).

51. The method and the use of claim 37, wherein the biomarker is p21.

52. The method and the use of claim 37, wherein the biomarker is p27.

53. The method and the use of claim 37, wherein the biomarker is pRb1.

54. The method and the use of claim 38, wherein the biomarker is soluble CD25 (sCD25).

55. The method and the use of claim 38, wherein the biomarker is IL-2.

56. The method and the use of claim 38, wherein the biomarker is TNFα.

57. The method and the use of claim 38, wherein the biomarker is IFNγ.

58. The method and the use of claim 38, wherein the biomarker is T-cell receptor (TCR) clonality.

59. The method and the use of claim 58, wherein the biomarker is measured by DNA sequencing of the TCR.

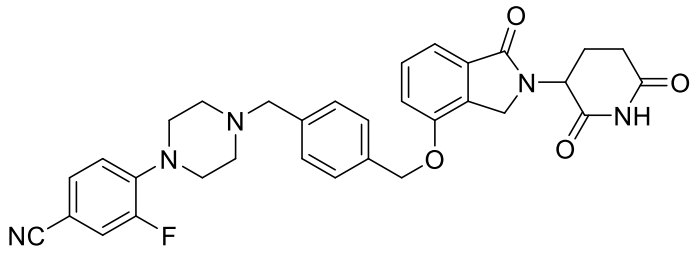
60. A method of identifying a subject with multiple myeloma that is relapsed, refractory, or resistant to conventional therapy who is likely to be responsive to a treatment compound, comprising:

(a) obtaining a sample from a subject;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is lower than a reference level of the biomarker;

wherein the treatment compound is a compound of Compound 1:



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

wherein the biomarker comprises CRBN.

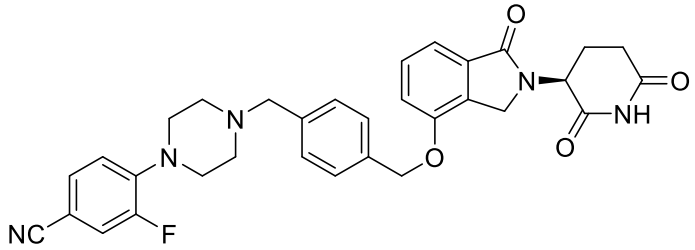
61. A method of identifying a subject with multiple myeloma that is relapsed, refractory, or resistant to conventional therapy who is likely to be responsive to a treatment compound, comprising:

(a) obtaining a sample from a subject;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is lower than a reference level of the biomarker;

wherein the treatment compound is a compound of Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises CRBN.

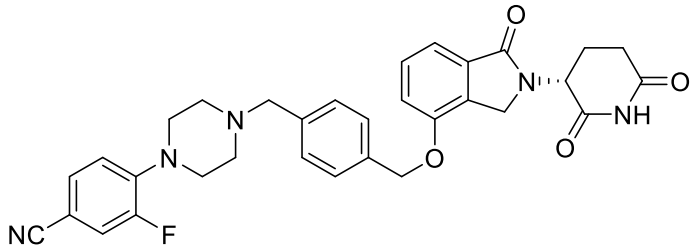
62. A method of identifying a subject with multiple myeloma that is relapsed, refractory, or resistant to conventional therapy who is likely to be responsive to a treatment compound, comprising:

(a) obtaining a sample from a subject;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is lower than a reference level of the biomarker;

wherein the treatment compound is a compound of Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises CRBN.

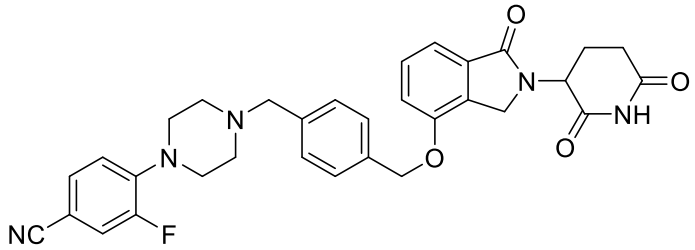
63. A method of predicting the responsiveness of a subject having multiple myeloma to a treatment compound, comprising:

(a) obtaining a sample from a subject;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is lower than a reference level of the biomarker;

wherein the treatment compound is a compound of Compound 1:



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

wherein the biomarker comprises CRBN.

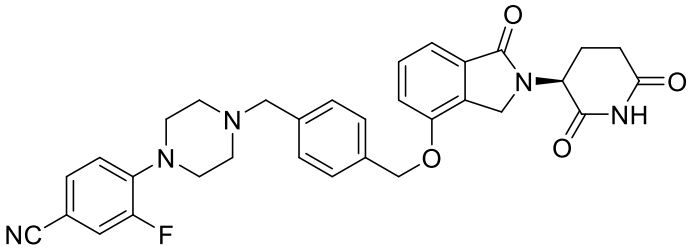
64. A method of predicting the responsiveness of a subject having multiple myeloma to a treatment compound, comprising:

(a) obtaining a sample from a subject;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is lower than a reference level of the biomarker;

wherein the treatment compound is a compound of Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises CRBN.

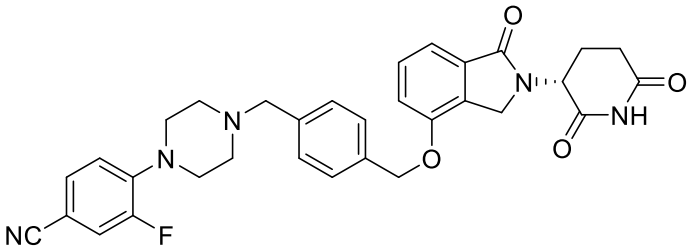
65. A method of predicting the responsiveness of a subject having multiple myeloma to a treatment compound, comprising:

(a) obtaining a sample from a subject;

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

(c) diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is lower than a reference level of the biomarker;

wherein the treatment compound is a compound of Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker comprises CRBN.

66. The method of any one of claims 60-65, comprising diagnosing the subject as being likely to be responsive to the treatment compound if the level of the biomarker in the sample is lower than the reference of the biomarker.

67. The method of any one of claims 60-65, comprising diagnosing the subject as being likely to be responsive to the treatment compound if the biomarker is detectable in the sample.

68. The method of any one of claims 1-57 or 60-67, wherein the level of the biomarker is measured by determining the protein level of the biomarker.

69. The method of any one of claims 1-57 or 60-67, wherein the level of the biomarker is measured by determining the mRNA level of the biomarker.

70. The method of any one of claims 1-57 or 60-67, wherein the level of the biomarker is measured by determining the cDNA level of the biomarker.

71. The method of any one of claims 1-57 or 60-67, wherein the biomarker is determined by RNA-sequencing (RNA-seq).

72. The method of claim 68, comprising contacting proteins within the sample with a first antibody that immunospecifically binds to the biomarker protein.

73. The method of claim 69, further comprising:

(a) contacting the biomarker protein bound to the first antibody with a second antibody with a detectable label, wherein the second antibody immunospecifically binds to the biomarker protein, and wherein the second antibody immunospecifically binds to a different epitope on the biomarker protein than the first antibody;

(b) detecting the presence of the second antibody bound to the biomarker protein; and

(c) determining the amount of the biomarker protein based on the amount of detectable label in the second antibody.

74. The method of claim 70, further comprising:

(a) contacting the first antibody bound to the biomarker protein with a second antibody with a detectable label, wherein the second antibody immunospecifically binds to the first antibody;

(b) detecting the presence of the second antibody bound to the first antibody; and

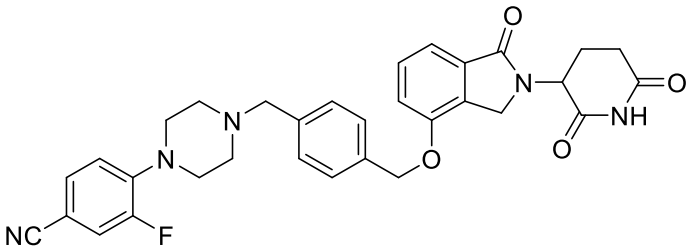
(c) determining the amount of the biomarker protein based on the amount of detectable label in the second antibody.

75. A method of determining or adjusting a dosage for treating a subject having multiple myeloma with a treatment compound comprising:

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

(b) determining the level of a biomarker in the one or more samples, and thereby determining if the dosage is appropriate or needs an adjustment;

wherein the treatment compound is a compound of Compound 1:



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

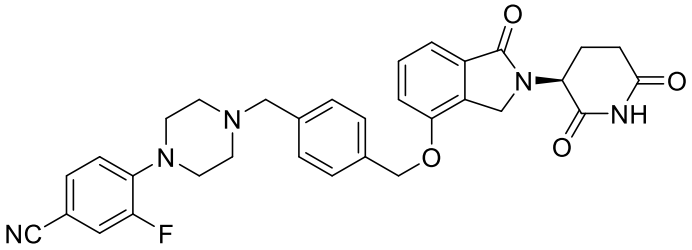
wherein the biomarker comprises IKZF1 and/or IKZF3.

76. A method of determining or adjusting a dosage for treating a subject having multiple myeloma with a treatment compound comprising:

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

(b) determining the level of a biomarker in the one or more samples, and thereby determining if the dosage is appropriate or needs an adjustment;

wherein the treatment compound is a compound of Compound 2:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

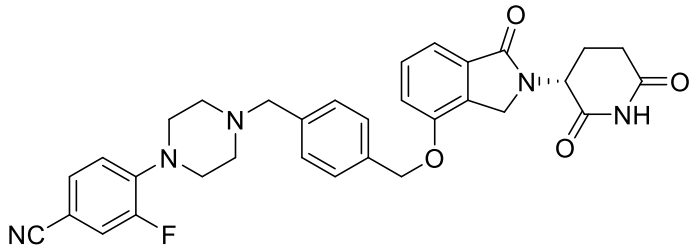
wherein the biomarker comprises IKZF1 and/or IKZF3.

77. A method of determining or adjusting a dosage for treating a subject having multiple myeloma with a treatment compound comprising:

(a) obtaining one or more samples from the subject who has been administered with the treatment compound at different time points; and

(b) determining the level of a biomarker in the one or more samples, and thereby determining if the dosage is appropriate or needs an adjustment;

wherein the treatment compound is a compound of Compound 3:



or a tautomer, isotopolog, or pharmaceutically acceptable salt thereof, and

wherein the biomarker is comprises IKZF1 and/or IKZF3.

78. The method of any one of claims 75-77, wherein the biomarker is IKZF1.

79. The method of any one of claims 75-77, wherein the biomarker is IKZF3.