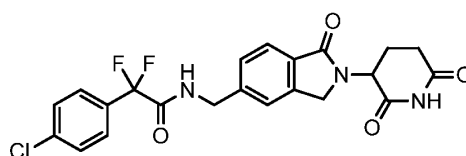


WHAT IS CLAIMED IS:

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

- i. providing a sample from the subject;
- ii. measuring gene expression level of one or more genes in the sample; and
- iii. identifying the subject as being likely to be responsive to the treatment comprising the compound if the expression level of the gene is different from a reference level,

wherein the compound is 2-(4-chlorophenyl)-N-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisindolin-5-yl)methyl)-2,2-difluoroacetamide (Compound D), which has the following structure:



or a stereoisomer or mixture of stereoisomers, isotopologue, pharmaceutically acceptable salt, tautomer, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, and

wherein the gene is a gene involved in mTOR signaling, or the gene is ILF2 or ILF3.

2. A method of treating a subject having cancer with a compound, comprising:

(a) identifying the subject having cancer that may be responsive to the treatment comprising the compound, comprising:

- i. providing a sample from the subject;
- ii. measuring gene expression level of one or more genes in the sample; and
- iii. identifying the subject as being likely to be responsive to the treatment comprising the compound if the expression level of the gene is different from a reference level,

(b) administering the subject a therapeutically effective amount of the compound if the subject is identified as being likely to be responsive to the treatment comprising the compound,

wherein the compound is Compound D, or a stereoisomer or mixture of stereoisomers, isotopologue, pharmaceutically acceptable salt, tautomer, solvate, hydrate, co-crystal, clathrate, or polymorph thereof and

wherein the gene is a gene involved in mTOR signaling, or the gene is ILF2 or ILF3.

3. The method of claim 1 or claim 2, wherein the gene is a gene involved in mTOR signaling.
4. The method of claim 3, wherein the gene is a positive regulator of mTOR signaling.
5. The method of claim 3, wherein the gene is mTOR.
6. The method of claim 3, wherein the gene is Raptor.
7. The method of claim 3, wherein the gene is Rictor.
8. The method of any one of claims 4-7, wherein the method comprises identifying the subject as being likely to be responsive to the treatment comprising the compound if the expression level of the gene is lower than a reference level.
9. The method of claim 8, wherein the reference level is the expression level of the gene in a subject resistant to Compound D.
10. The method of claim 8, wherein the reference level is the expression level of the gene in a subject without the cancer.
11. The method of claim 8, wherein the reference level is a pre-determined level.
12. The method of claim 3, wherein the gene is a negative regulator of mTOR signaling.
13. The method of claim 3, wherein the gene is TSC1

14. The method of claim 3, wherein the gene is TSC2.
15. The method of claim 3, wherein the gene is GCN1.
16. The method of claim 3, wherein the gene is GCN2.
17. The method of claim 3, wherein the gene is DDIT4.
18. The method of claim 3, wherein the gene is ATF4.
19. The method of any one of claims 12-18, wherein the method comprises identifying the subject as being likely to be responsive to the treatment comprising the compound if the expression level of the gene is higher than a reference level.
20. The method of claim 19, wherein the reference level is the expression level of the gene in a subject responsive to Compound D.
21. The method of claim 19, wherein the reference level is the expression level of the gene in a subject without the cancer.
22. The method of claim 19, wherein the reference level is a pre-determined level.
23. The method of claim 1 or claim 2, wherein the gene is ILF2.
24. The method of claim 1 or claim 2, wherein the gene is ILF3.
25. The method of claim 23 or claim 24, wherein the method comprises identifying the subject as being likely to be responsive to the treatment comprising the compound if the expression level of the gene is higher than a reference level.

26. The method of claim 25, wherein the reference level is the expression level of the gene in a subject responsive to Compound D.
27. The method of claim 25, wherein the reference level is the expression level of the gene in a subject without the cancer.
28. The method of claim 25, wherein the reference level is a pre-determined level.
29. The method of any one of claims 1 to 28, wherein the cancer is a hematological cancer.
30. The method of any one of claims 1 to 28, wherein the cancer is a lymphoma.
31. The method of any one of claim 1 to 28, wherein the cancer is a leukemia.
32. The method of claim 31, wherein the cancer is AML.
33. A method of identifying a subject having cancer who is likely to be responsive to a treatment comprising a compound or predicting the responsiveness of a subject having or suspected of having cancer to a treatment comprising the compound, comprising:
- i. providing a sample from the subject;
 - ii. determining a sequence of a biomarker in the sample; and
 - iii. identifying the subject as being unlikely to be responsive to the treatment comprising the compound if a mutation is identified in the biomarker, and/or identifying the subject as being likely to be responsive to the treatment comprising the compound if the mutation is not identified in the biomarker;
- wherein the compound is Compound D, or a stereoisomer or mixture of stereoisomers, isotopologue, pharmaceutically acceptable salt, tautomer, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, and
- wherein the biomarker is CRBN or GSPT1.

34. The method of claim 33, wherein the biomarker is GSPT1, and wherein the mutation is a mutation of amino acid residue C568, L569, V570, D571, K572, K573, S574, G575, or E576 of GSPT1.
35. The method of claim 34, wherein the mutation is selected from a group consisting of K572, K573, S574, G575, and combinations thereof.
36. The method of claim 35, wherein the mutation comprises G575N.
37. The method of claim 33, wherein the biomarker is CRBN, and wherein the mutation is a mutation of amino acid residue N351, H357, W380, Y384, W386, or W400.
38. The method of claim 37, wherein the mutation is Y384A or W386A.
39. A method of treating a subject having cancer comprising administering to the subject a compound, wherein the subject has been determined to be likely to be responsive to the compound according a method comprising:
- i. providing a sample from the subject;
 - ii. determining a sequence of a biomarker in the sample; and
 - iii. identifying the subject as being likely to be responsive to the compound if a mutation is not identified in the biomarker;
- wherein the compound is Compound D, or a stereoisomer or mixture of stereoisomers, isotopologue, pharmaceutically acceptable salt, tautomer, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, and
- wherein the biomarker is CRBN or GSPT1.
40. A method of treating a subject having cancer comprising administering to the subject a second compound, wherein the subject has been determined to be unlikely to be responsive to a first compound according a method comprising:
- i. providing a sample from the subject;
 - ii. determining a sequence of a biomarker in the sample; and

iii. identifying the subject as being unlikely to be responsive to the compound if a mutation is identified in the biomarker;

wherein the first compound is Compound D, or a stereoisomer or mixture of stereoisomers, isotopologue, pharmaceutically acceptable salt, tautomer, solvate, hydrate, co-crystal, clathrate, or polymorph thereof,

wherein the second compound is not Compound D, or a stereoisomer or mixture of stereoisomers, isotopologue, pharmaceutically acceptable salt, tautomer, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, and

wherein the biomarker is CRBN or GSPT1.

41. The method of claim 39 or claim 40, wherein the biomarker is GSPT1, and wherein the mutation is a mutation of amino acid residue C568, L569, V570, D571, K572, K573, S574, G575, or E576 of GSPT1.

42. The method of claim 41, wherein the mutation is selected from a group consisting of K572, K573, S574, G575, and combinations thereof.

43. The method of claim 42, wherein the mutation comprises G575N.

44. The method of claim 39 or claim 40, wherein the biomarker is CRBN, and wherein the mutation is a mutation of amino acid residue N351, H357, W380, Y384, W386, or W400.

45. The method of claim 44, wherein the mutation is Y384A or W386A.

46. The method of any one of claims 33 to 45, wherein the cancer is a hematological cancer.

47. The method of any one of claims 33 to 45, wherein the cancer is a lymphoma.

48. The method of any one of claim 33 to 45, wherein the cancer is a leukemia.

49. The method of any one of claims 33 to 45, wherein the cancer is AML.