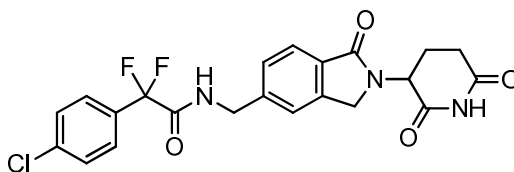


WHAT IS CLAIMED IS:

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

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

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

(b) ~~administering the subject~~ a therapeutically effective amount of the compound is to be administered to the subject 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 the use claim 2, wherein the gene is a gene involved in mTOR signaling.

4. The method or use of claim 3, wherein the gene is a positive regulator of mTOR signaling.

5. The method or use of claim 3, wherein the gene is mTOR.

6. The method or use of claim 3, wherein the gene is Raptor.

7. The method or use of claim 3, wherein the gene is Rictor.

8. The method or use 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 is to be identified if the expression level of the gene is lower than a reference level.

9. The method or use of claim 8, wherein the reference level is the expression level of the gene in a subject resistant to Compound D.

10. The method or use of claim 8, wherein the reference level is the expression level of the gene in a subject without the cancer.

11. The method or use of claim 8, wherein the reference level is a pre-determined level.

12. The method or use of claim 3, wherein the gene is a negative regulator of mTOR signaling.
13. The method or use of claim 3, wherein the gene is TSC1.
14. The method or use of claim 3, wherein the gene is TSC2.
15. The method or use of claim 3, wherein the gene is GCN1.
16. The method or use of claim 3, wherein the gene is GCN2.
17. The method or use of claim 3, wherein the gene is DDIT4.
18. The method or use of claim 3, wherein the gene is ATF4.
19. The method or use 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 is to be identified if the expression level of the gene is higher than a reference level.
20. The method or use of claim 19, wherein the reference level is the expression level of the gene in a subject responsive to Compound D.
21. The method or use of claim 19, wherein the reference level is the expression level of the gene in a subject without the cancer.
22. The method or use of claim 19, wherein the reference level is a pre-determined level.
23. The method of claim 1 or the use of claim 2, wherein the gene is ILF2.
24. The method of claim 1 or the use of claim 2, wherein the gene is ILF3.

25. The method or use 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 is to be identified if the expression level of the gene is higher than a reference level.

26. The method or use of claim 25, wherein the reference level is the expression level of the gene in a subject responsive to Compound D.

27. The method or use of claim 25, wherein the reference level is the expression level of the gene in a subject without the cancer.

28. The method or use of claim 25, wherein the reference level is a pre-determined level.

29. The method or use of any one of claims 1 to 28, wherein the cancer is a hematological cancer.

30. The method or use of any one of claims 1 to 28, wherein the cancer is a lymphoma.

31. The method or use of any one of claim 1 to 28, wherein the cancer is a leukemia.

32. The method or use 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. Use of a compound in the manufacture of a medicament for~~A method of treating a~~ subject having cancer ~~comprising administering to the subject a compound~~, wherein:

_____ (a) the subject has been determined to that may be likely to be responsive to the compound is to be determined, wherein~~according a method comprising:~~

- i. ~~providing~~ a sample from the subject is to be provided;
- ii. ~~determining~~ a sequence of a biomarker in the sample is to be determined; and
- iii. ~~identifying~~ the subject as being likely to be responsive to the compound is to be identified if a mutation is not identified in the biomarker;

_____ (b) the compound is to be administered to the subject if the subject is identified as being likely to be responsive to 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 biomarker is CRBN or GSPT1.

40. ~~Use of a second compound in the manufacture of a medicament for~~ A method of treating a subject having cancer ~~comprising administering to the subject a second compound~~, wherein:

~~_____ (a) the subject has been determined to that may be unlikely to be responsive to a first compound is to be determined, wherein~~ _____ (a) the subject is to be unlikely to be responsive to a first compound is to be determined, wherein ~~according a method comprising:~~

- i. ~~providing~~ providing a sample from the subject is to be provided;
- ii. ~~determining~~ determining a sequence of a biomarker in the sample is to be determined; and
- iii. ~~identifying~~ identifying the subject as being unlikely to be responsive to the first compound is to be identified if a mutation is identified in the biomarker;

~~_____ (b) the second compound is to be administered to the subject if the subject is identified as~~ _____ (b) the second compound is to be administered to the subject if the subject is identified as being unlikely to be responsive to the first compound,

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-use~~ use 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-use~~ use of claim 41, wherein the mutation is selected from a group consisting of K572, K573, S574, G575, and combinations thereof.

43. The ~~usemethod~~ use of claim 42, wherein the mutation comprises G575N.

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

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

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

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

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