WHAT IS CLAIMED IS:

1. Use of a CDK2 inhibitor in the manufacture of a medicament for the treatment of a human subject having a cyclin-dependent kinase 2 (CDK2)-associated cancer, wherein the human subject has been previously determined to:

(i)

(a) have a nucleotide sequence encoding a p16 protein comprising the amino acid sequence of SEQ ID NO:1;

(b) have a cyclin dependent kinase inhibitor 2A (CDKN2A) gene lacking one or more inactivating nucleic acid substitutions and/or deletions; and/or

(c) express a p16 protein; and

(ii)

(a) have an amplification of the cyclin E1 (CCNE1) gene; and/or

(b) have an expression level of CCNE1 in a biological sample obtained from the human subject that is higher than a control expression level of CCNE1;

wherein the control expression level of CCNE1 is the expression level of CCNE1 in a sample or samples obtained from one or more subjects that have not responded to treatment with the CDK2 inhibitor; and

wherein the CDK2 inhibitor is:

4-((8-cyclopentyl-6,6-dimethyl-7-oxo-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-2-yl)amino)benzenesulfonamide,

8-cyclopentyl-6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-d]pyrimidin-7(6H)-one,

6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-8-phenyl-5,8-dihydropyrido[2,3-d]pyrimidin-7(6H)-one,

8-(1,1-difluorobutan-2-yl)-6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

6,6-dimethyl-8-((1-methyl-1*H*-pyrazol-5-yl)methyl)-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-8-(tetrahydrofuran-3-yl)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

8-((1R,2R)-2-hydroxy-2-methylcyclopentyl)-2-((1-(methylsulfonyl)piperidin-4-yl)amino)pyrido[2,3-d]pyrimidin-7(8H)-one,

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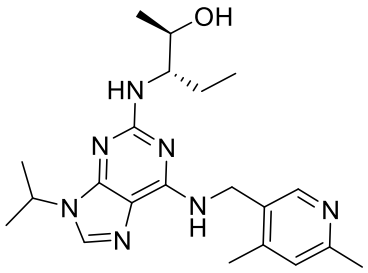
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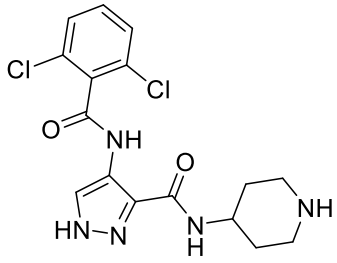
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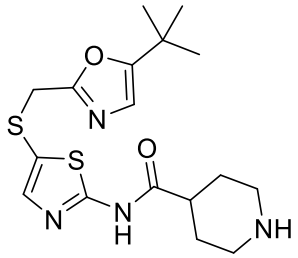
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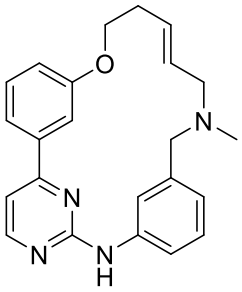
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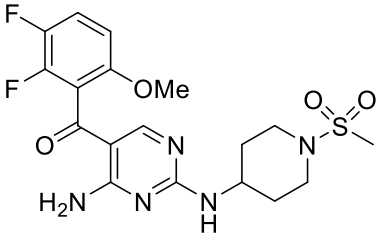
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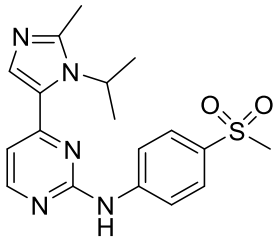
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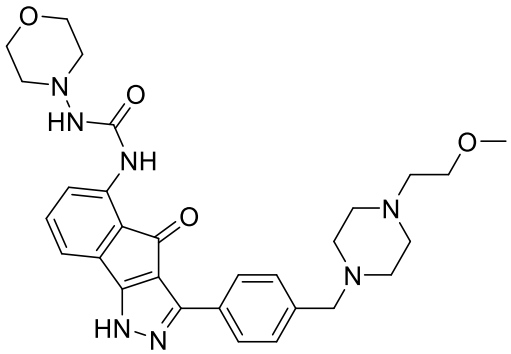
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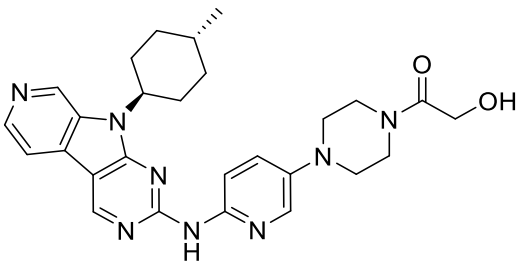
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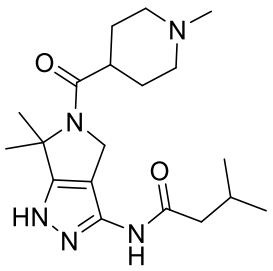
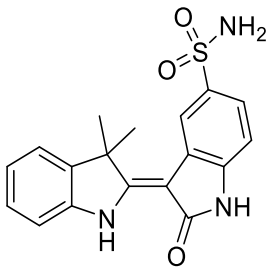
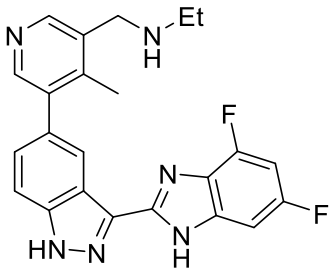
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PHA-793887 , ZK-304709 , or AG-24322 ,

or a pharmaceutically acceptable salt thereof.

2. The use of claim 1, wherein the human subject has been previously determined to:

(i)

(a) have a nucleotide sequence encoding a p16 protein comprising the amino acid sequence of SEQ ID NO:1; and/or

(b) a CDKN2A gene lacking one or more inactivating nucleic acid substitutions and/or deletions; and

(ii) have an amplification of the CCNE1 gene in a biological sample obtained from the human subject.

3. The use of claim 1, wherein the expression level of CCNE1 in the biological sample is at least 1.5, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 20, at least 25, at least 50, at least 75, or at least 100 times higher than the control expression level of CCNE1.

4. The use of any one of claims 1-3, wherein the CDKN2A gene encodes a protein comprising the amino acid sequence of SEQ ID NO:1.

5. Use of a CDK2 inhibitor in the manufacture of a medicament for the treatment of a human subject having a cyclin-dependent kinase 2 (CDK2)-associated cancer, wherein:

(i) in a biological sample obtained from the human subject:

(a) a nucleotide sequence encoding a p16 protein comprising the amino acid sequence of SEQ ID NO:1 is present;

(b) a cyclin dependent kinase inhibitor 2A (CDKN2A) gene lacking one or more inactivating nucleic acid substitutions is present; and/or

(c) a p16 protein is present; and

(ii) in a biological sample obtained from the human subject:

(a) there is present an amplification of the cyclin E1 (CCNE1) gene; and/or

(b) there is present an expression level of CCNE1 that is higher than a control expression level of CCNE1;

wherein the control expression level of CCNE1 is the expression level of CCNE1 in a sample or samples obtained from one or more subjects that have not responded to treatment with the CDK2 inhibitor; and

wherein the CDK2 inhibitor is:

4-((8-cyclopentyl-6,6-dimethyl-7-oxo-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-2-yl)amino)benzenesulfonamide,

8-cyclopentyl-6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-d]pyrimidin-7(6H)-one,

6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-8-phenyl-5,8-dihydropyrido[2,3-d]pyrimidin-7(6H)-one,

8-(1,1-difluorobutan-2-yl)-6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

6,6-dimethyl-8-((1-methyl-1*H*-pyrazol-5-yl)methyl)-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-8-(tetrahydrofuran-3-yl)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

8-((1R,2R)-2-hydroxy-2-methylcyclopentyl)-2-((1-(methylsulfonyl)piperidin-4-yl)amino)pyrido[2,3-d]pyrimidin-7(8H)-one,

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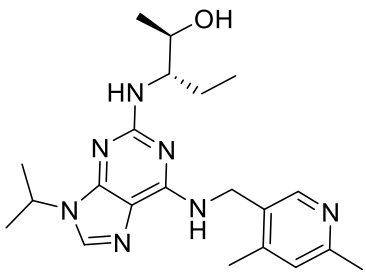
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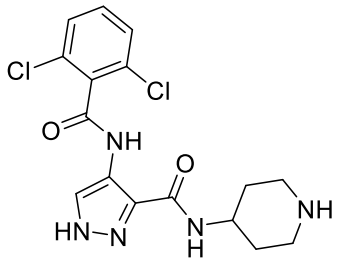
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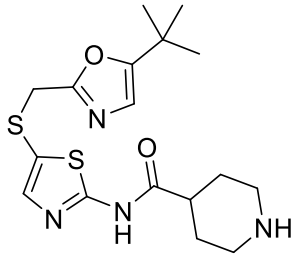
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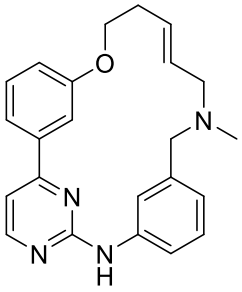
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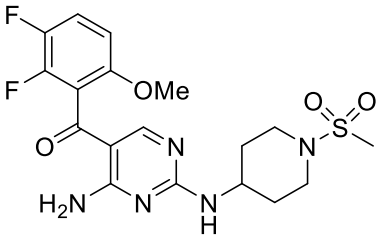
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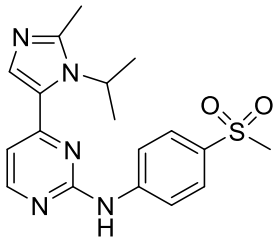
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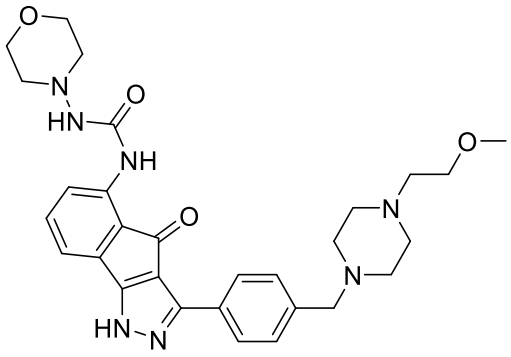
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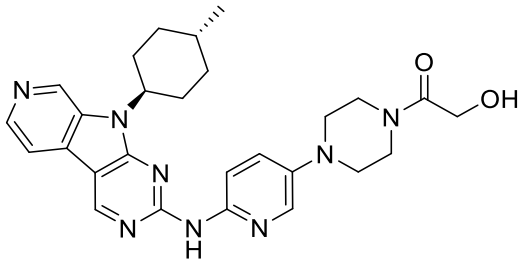
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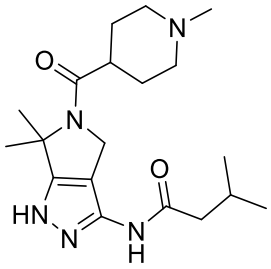
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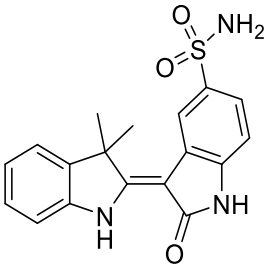


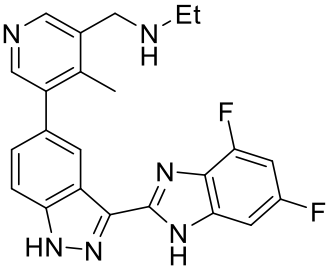
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PHA-793887, ZK-304709, or AG-24322,

or a pharmaceutically acceptable salt thereof.

6. The use of claim 5, comprising:

(i) in a biological sample obtained from the human subject:

(a) a nucleotide sequence encoding a p16 protein comprising the amino acid sequence of SEQ ID NO:1 is present;

(b) a CDKN2A gene lacking one or more inactivating nucleic acid substitutions and/or deletions is present; and/or

(c) a p16 protein is present; and

(d) there is present an amplification of the CCNE1 gene.

7. The use of claim 5, wherein the expression level of CCNE1 in the biological sample is at least 1.5, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 20, at least 25, at least 50, at least 75, or at least 100 times higher than the control expression level of CCNE1.

8. The use of any one of claims 5-7, wherein the CDKN2A gene encodes a protein comprising the amino acid sequence of SEQ ID NO:1.

9. The use of any one of claims 1-8, wherein the medicament comprises a second therapeutic agent.

10. The use of claim 9, wherein the second therapeutic agent is a BCL2 inhibitor or a CDK4/6 inhibitor.

11. An *in vitro* method of predicting the response of a human subject having a cyclin-dependent kinase 2 (CDK2)-associated cancer to a CDK2 inhibitor, comprising:

(i) determining, from a biological sample obtained from the human subject:

(a) the nucleotide sequence of a cyclin dependent kinase inhibitor 2A (CDKN2A) gene;

(b) the presence of a CDKN2A gene lacking one or more inactivating nucleic acid substitutions and/or deletions; and/or

(c) the presence of a p16 protein; and

(ii) determining, from a biological sample obtained from the human subject:

(a) the copy number of the cyclin E1 (CCNE1) gene; and/or

(b) the expression level of CCNE1,

wherein

(1)

(a) the presence of a CDKN2A gene encoding a p16 protein comprising the amino acid sequence of SEQ ID NO:1;

(b) the presence of a CDKN2A gene lacking one or more inactivating nucleic acid substitutions and/or deletions; and/or

(c) the presence of a p16 protein; and

(2) an amplification of the CCNE1 gene and/or an expression level of CCNE1 that is higher than a control expression level of CCNE1,

is predictive that the human subject will respond to the CDK2 inhibitor;

wherein the control expression level of CCNE1 is the expression level of CCNE1 in a sample or samples obtained from one or more subjects that have not responded to treatment with the CDK2 inhibitor; and

wherein the CDK2 inhibitor is:

4-((8-cyclopentyl-6,6-dimethyl-7-oxo-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-2-yl)amino)benzenesulfonamide,

8-cyclopentyl-6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-d]pyrimidin-7(6H)-one,

6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-8-phenyl-5,8-dihydropyrido[2,3-d]pyrimidin-7(6H)-one,

8-(1,1-difluorobutan-2-yl)-6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

6,6-dimethyl-8-((1-methyl-1*H*-pyrazol-5-yl)methyl)-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

6,6-dimethyl-2-((1-(methylsulfonyl)piperidin-4-yl)amino)-8-(tetrahydrofuran-3-yl)-5,8-dihydropyrido[2,3-*d*]pyrimidin-7(6*H*)-one,

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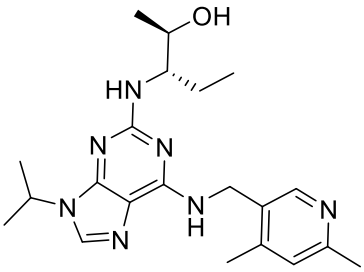
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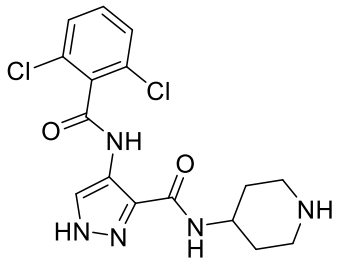
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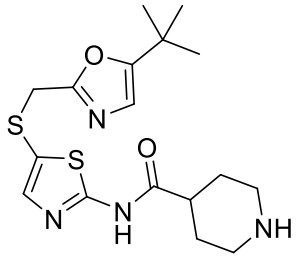
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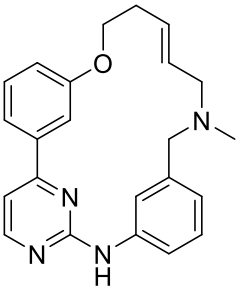
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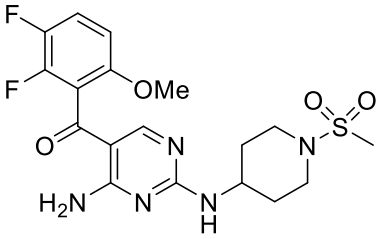
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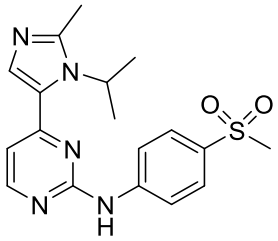
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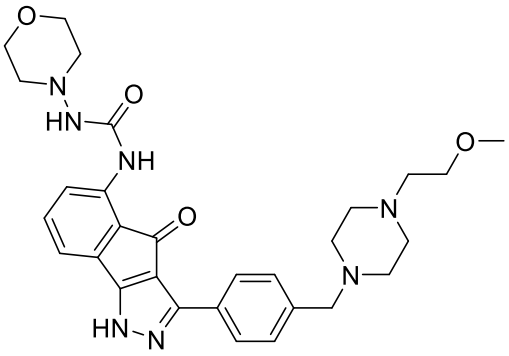
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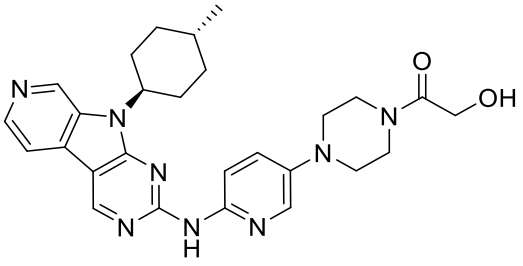
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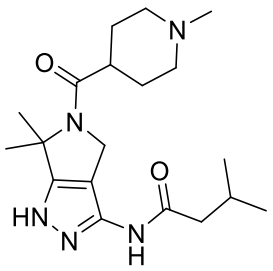
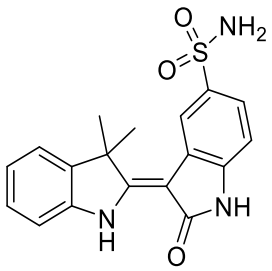
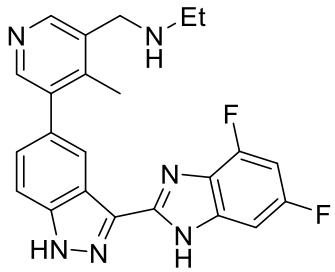
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PHA-793887 , ZK-304709 , or AG-24322 ,

or a pharmaceutically acceptable salt thereof.

12. The method of claim 11, comprising:

(i) determining, from a biological sample obtained from the human subject:

(a) the nucleotide sequence of a CDKN2A gene and/or the presence of a CDKN2A gene lacking one or more inactivating nucleic acid substitutions and/or deletions; and

(ii) determining, from a biological sample obtained from the human subject:

(a) the copy number of the CCNE1 gene,

wherein

(1)

(a) the presence of a CDKN2A gene encoding a p16 protein comprising the amino acid sequence of SEQ ID NO:1; and/or the

(b) presence of a CDKN2A gene lacking one or more inactivating nucleic acid substitutions and/or deletions, and

(2) an amplification of the CCNE1 gene,

is predictive that the human subject will respond to the CDK2 inhibitor.

13. The use of any one of claims 1-10 or the method of claim 11 or 12, wherein the amplification of the CCNE1 gene comprises a gene copy number of at least 3; at least 5; or at least 21.

14. The use of any one of claims 1-10, and 13 or the method of any one of claims 11-13, wherein the expression level of CCNE1 is the expression level of CCNE1 mRNA; or wherein the expression level of CCNE1 is the expression level of CCNE1 protein.

15. The use of claim 14, or the method of claim 14, wherein the expression level of CCNE1 is measured by RNA sequencing, quantitative polymerase chain reaction (PCR), in situ hybridization, nucleic acid array or RNA sequencing; or wherein the expression level of CCNE1 is measured by western blot, enzyme-linked immunosorbent assay, or immunohistochemistry staining.

16. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15, wherein the CDK2-associated cancer is lung squamous cell carcinoma, lung adenocarcinoma, pancreatic adenocarcinoma, breast invasive carcinoma, uterine carcinosarcoma, ovarian serous cystadenocarcinoma, stomach adenocarcinoma, esophageal carcinoma, bladder urothelial carcinoma, mesothelioma, or sarcoma.

17. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15, wherein the CDK2-associated cancer is lung adenocarcinoma, breast invasive carcinoma, uterine carcinosarcoma, ovarian serous cystadenocarcinoma, or stomach adenocarcinoma.

18. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15, wherein the CDK2-associated cancer is an adenocarcinoma, carcinoma, or cystadenocarcinoma.

19. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15, wherein the CDK2-associated cancer is uterine cancer, ovarian cancer, stomach cancer, esophageal cancer, lung cancer, bladder cancer, pancreatic cancer, or breast cancer.

20. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15, wherein the CDK2-associated cancer is ovarian cancer, uterine carcinosarcoma, or breast cancer.

21. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15, wherein the CDK2-associated cancer is endometrial cancer.

22. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15,

wherein the CDK2-associated cancer comprises p27 inactivation.

23. The use of any one of claims 1-10 and 13-15 or the method of any one of claims 11-15, wherein the CDK2-associated cancer is a N-myc amplified neuroblastoma, a K-Ras mutant lung cancer, or a cancer with a FBW7 mutation and CCNE1 overexpression.