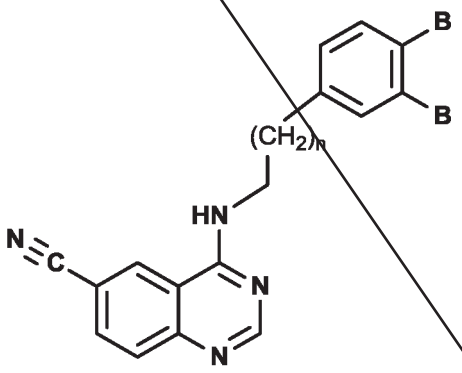
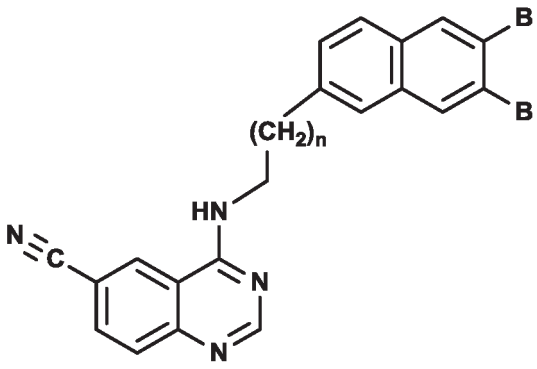
What is claimed is:

1. A small molecule compound that specifically inhibits CDK8 and CDK19, with the proviso that the small molecule compound is not cortistatin A or a small molecule compound disclosed in US20080033000 or US20120071477.

2. The small molecule compound according to claim 1, having the structural formula **I** or **II**:

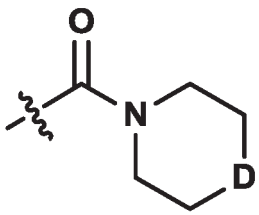


I



II

wherein each B is independently hydrogen or



provided that at least one B is hydrogen and not more than one B is hydrogen;

D is selected from -NH, -N-lower alkyl, or O;

and n is 0-2.

3. The small molecule compound according to claim 1, wherein lower alkyl is methyl.

4. The small molecule compound according to claim 1, wherein n is 0 or 1.

5. The small molecule compound according to claim 1, wherein n is 1.

6. The small molecule compound according to claim 1, selected from the group consisting of SNX2-1-162, SNX2-1-163, SNX2-1-164, SNX2-1-165, SNX2-1-166 and SNX2-1-167.

7. The small molecule compound SNX2-1-165.

8. The small molecule compound according to claim 1, selected from the group of structures shown in Figure 1.

9. A pharmaceutical formulation comprising the compound according to any of claims 1-8 and a physiologically acceptable carrier or diluent.

10. A method for therapeutically treating a mammal having a CDKI-mediated disease comprising administering to the mammal a therapeutically effective amount of a pharmaceutical formulation according to claim 9.

11. The method according to claim 10, wherein the CDKI-mediated disease is selected from Alzheimer's disease, other dementias, amyloidosis, atherosclerosis, renal disease, viral diseases, and cancer.

12. The method according to claim 11, wherein the disease is cancer or HIV infection.

13. A method for treating a cancer in a patient that is a tumor that expresses β-catenin, comprising administering to the patient a small molecule compound according to any of claims 2-8.

14. A method for chemoprotecting a patient at risk for developing cancer, comprising administering to the patient a specific inhibitor of CDK8/19.

15. A method for preventing cancer recurrence or metastasis in a cancer patient who has undergone debulking treatment for a tumor, comprising administering to the patient a small molecule compound that specifically inhibits CDK8/19 following debulking.

16. The method according to claim 15, wherein the patient is an ovarian or breast cancer patient.

17. A method for preventing tumor invasion, comprising administering to the patient a small molecule compound that specifically inhibits CDK8/19.

18. A method for treating a cancer patient comprising administering to the patient a small molecule compound that specifically inhibits CDK8/19 in combination with a DNA damaging agent.

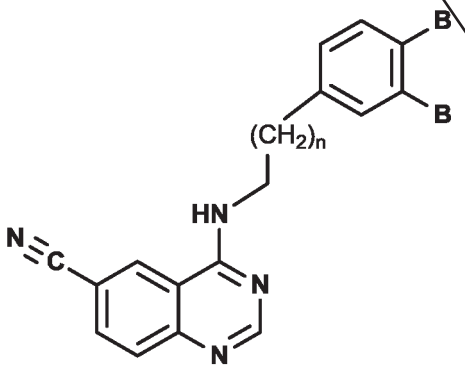
19. The method according to claim 18, wherein the patient is an ovarian or breast cancer patient.

20. A method for inhibiting tumor-promoting factor secretion by one or more of fibroblasts and stromal cells in a patient, wherein the secretion is induced by a DNA-damaging agent, comprising administering to the patient a small molecule compound that specifically inhibits CDK8/19.

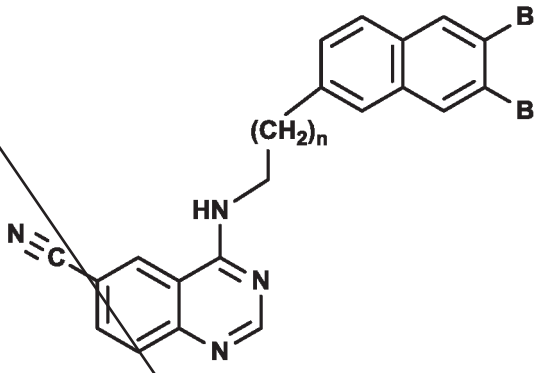
21. A method for improving the efficacy of adjuvant therapy given to a patient in combination with surgery, comprising administering a small molecule compound that specifically inhibits CDK8/19 in combination with the adjuvant therapy.

22. A method for treating breast cancer in a patient, comprising administering to the patient a small molecule compound that specifically inhibits CDK8/19.

23. The method according to any of claims 10-21, wherein the small molecule compound has the structural formula **I** or **II**:

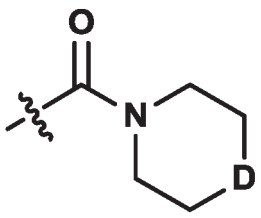


I



II

wherein each B is independently hydrogen or



provided that at least one B is hydrogen and not more than one B is hydrogen;

D is selected from -NH, -N-lower alkyl, or O;

and n is 0-2.

24. The method according to claim 23, wherein lower alkyl is methyl.

25. The method according to claim 23, wherein n is 0 or 1.

26. The method according to claim 21, wherein the small molecule compound that specifically inhibits CDK8/19 is selected from the group consisting of SNX2-1-162, SNX2-1-163, SNX2-1-164, SNX2-1-165, SNX2-1-166 and SNX2-1-167.

27. The method according to claim 25, wherein the small molecule compound that specifically inhibits CDK8/19 is SNX2-1-165.

28. The method according to any of claims 10-21, wherein the small molecule compound that specifically inhibits CDK8/19 is selected from the compounds shown in Figure 1.

29. The method according to claim 22, wherein the specific inhibitor of CDK8/19 is administered orally.

30. The method according to claim 28, wherein the specific inhibitor of CDK8/19 is administered orally.

31. A method for determining whether a cancer patient is suitable to be treated with a DNA-damaging agent, the method comprising determining whether one or more of CDK8, CCNC and CDK19 is overexpressed in a tumor sample from the pateient.

32. The method according to claim 31, wherein it is determined whether CDK8 is overexpressed in the tumor sample.

33. The method according to claim 31, wherein the patient is an ovarian or breast cancer patient.

34. A method for determining the likelihood of recurrence or metastasis of a tumor in a cancer patient, comprising determining whether one or more of CDK8, CCNC and CDK19 is overexpresssed in a tumor sample from the patient.

35. The method according to claim 34, wherein it is determined whether CDK8 is overexpressed in the tumor sample.

36. The method according to claim 34, wherein the patient is an ovarian or breast cancer patient.

37. A method for determining whether a surgical cancer patient will benefit from adjuvant therapy, comprising determining whether one or more of CDK8, CCNC and CDK19 is overexpressed in a tumor sample from the patient.

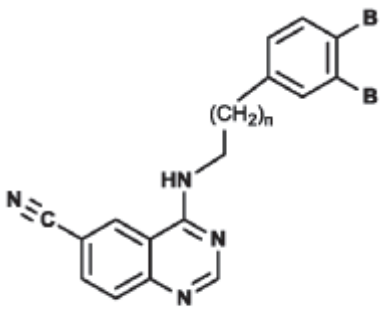
38. The method according to claim 37, wherein it is determined whether CDK8 is overexpressed in the tumor sample.

39. The method according to claim 34, wherein the patient is an ovarian or breast cancer patient.

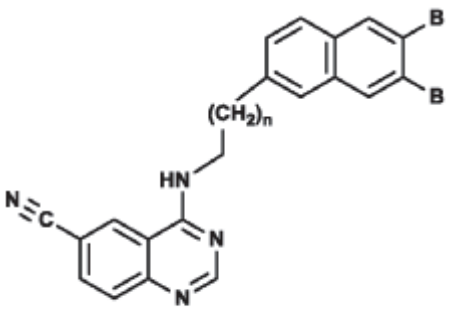
CLAIMS

What is claimed is:

1. A small molecule compound that specifically inhibits CDK8 and CDK19 having the structural formula I or II:

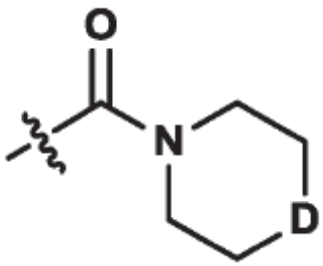


I



II

wherein each B is independently hydrogen or



provided that at least one B is hydrogen and not more than one B is hydrogen;

D is selected from -NH, -N-lower alkyl, or O;

and n is 0-2.

2. The small molecule compound according to claim 1, wherein lower alkyl is methyl.

3. The small molecule compound according to claim 1, wherein n is 0 or 1.

4. The small molecule compound according to claim 1, selected from the group consisting of SNX2-1-150, SNX2-1-151, SNX2-1-152, SNX2-1-153, SNX2-1-154, SNX2-1-155, SNX2-1-157, SNX2-1-158, SNX2-1-162, SNX2-1-163, SNX2-1-164, SNX2-1-165, SNX2-1-166 and SNX2-1-167.

5. A pharmaceutical formulation comprising the compound according to any of claims 1 to 4 and a physiologically acceptable carrier or diluent.

6. Use of a therapeutically effective amount of a pharmaceutical formulation according to claim 5 in the manufacture of a medicament for treating a mammal having a CDKI-mediated disease.

7. The use according to claim 6, wherein the CDKI-mediated disease is selected from the group consisting of Alzheimer's disease, other dementias, amyloidosis, atherosclerosis, renal disease, viral diseases, cancer and HIV infection.

8. Use of a small molecule compound according to any of claims 1 to 4 in the manufacture of a medicament for treating a tumor that expresses β-catenin in a patient.

9. Use of a small molecule compound that specifically inhibits CDK8/19 according to any of claims 1 to 4 for chemoprotecting a patient at risk for developing cancer.

10. Use of a small molecule compound according to any of claims 1 to 4 that specifically inhibits CDK8/19 following debulking for preventing cancer recurrence or metastasis in a patient who has undergone debulking treatment for a tumor.

11. The use according to claim 10, wherein the cancer is an ovarian or breast cancer.

12. Use of a small molecule compound that specifically inhibits CDK8/19 according to any of claims 1 to 4 for preventing tumor invasion in a patient.

13. Use of a small molecule compound according to any of claims 1 to 4 that specifically inhibits CDK8/19 in combination with a DNA damaging agent in the manufacture of a medicament for treating cancer in a patient.

14. The use according to claim 13, wherein the cancer is an ovarian or breast cancer.

15. Use of a small molecule compound that specifically inhibits CDK8/19 according to any of claims 1 to 4 for inhibiting tumor-promoting factor secretion by one or more of fibroblasts and stromal cells in a patient, wherein the secretion is induced by a DNA-damaging agent.

16. Use of a small molecule compound according to any of claims 1 to 4 that specifically inhibits CDK8/19 in combination with an adjuvant therapy for improving the efficacy of adjuvant therapy given to a patient in combination with surgery.

17. Use of a small molecule compound that specifically inhibits CDK8/19 according to any of claims 1 to 4 in the manufacture of a medicament for treating breast cancer in a patient.

18. The use according to any of claims 6 to 17, wherein the small molecule compound that specifically inhibits CDK8/19 is administered orally.