compositions may also be contained within a single, undivided container. Typically, the kit comprises directions for the administration of the separate components. The kit form is particularly advantageous when the separate components are preferably administered in different dosage forms (e.g., oral and parenteral), are administered at different dosage intervals, or when titration of the individual components of the combination is desired by the prescribing physician.

SPECIFIC ASPECTS OF THE INVENTION

In one specific aspect of the invention the hyperproliferative disorder is cancer.

In one specific aspect of the invention the cancer is associated with PTEN mutation.

In one specific aspect of the invention the cancer is associated with AKT mutation, overexpression or amplification.

In one specific aspect of the invention the cancer is associated with PI3K mutation.

In one specific aspect of the invention the cancer is associated with a HER2 mutation.

In one specific aspect of the invention the cancer is selected from, breast, lung, ovarian, prostate (e.g., castration resistant prostate cancer), melanoma, gastric, colon, renal, head and neck, and ~~gilomaglioma~~.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and 5-FU are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof, 5-FU, and oxaliplatin are administered to the mammal and the cancer is gastric, ovarian, or colon.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof, 5-FU, and oxaliplatin are administered to the mammal and the cancer is gastric, prostate, head or neck.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof, 5-FU, oxaliplatin, and folinic acid are administered to the mammal and the cancer is gastric, ovarian, or colon.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof, 5-FU, oxaliplatin, and folinic acid are administered to the mammal and the cancer is gastric, prostate, head or neck.

In one specific aspect of the invention the compound of formula I, e.g., GDC-0068, or a pharmaceutically acceptable salt thereof, and one or more of 5-FU, oxaliplatin, and folinic acid are administered to the mammal to treat cancer and the cancer is HER2 negative gastric (e.g., first line), colorectal (e.g., first line, optionally in combination with a VEGF inhibitor,

such as bevacizumab), SCC head/neck (e.g., first line), colorectal (e.g., second line), or pancreatic (e.g., second line).

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and carboplatin are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and carboplatin are administered to the mammal and the cancer is breast, lung, or prostate.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and carboplatin are administered to the mammal and the cancer is breast, lung, prostate, head or neck.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and irinotecan are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and irinotecan are administered to the mammal and the cancer is colon.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and paclitaxel are administered to the mammal to treat endometrial cancer (e.g., second line).

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and docetaxel are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and docetaxel are administered to the mammal and the cancer is breast, ~~gilomaglioma~~, lung, melanoma, ovarian, or prostate.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and docetaxel are administered to the mammal and the cancer is breast, ovarian, or prostate.

In one specific aspect of the invention the compound of formula I, e.g., GDC-0068, or a pharmaceutically acceptable salt thereof and docetaxel are administered to the mammal and the cancer is castration resistant prostate (e.g., first line), HER2 negative breast (e.g., first line), gastric (e.g., second line), gastroesophageal junction (e.g., second line), non-small cell lung (e.g., second line), ovarian (e.g., second line), and squamous cell carcinoma head and neck (e.g., second line).

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and doxorubicin are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and doxorubicin are administered to the mammal and the cancer is breast, lung, ovarian, ~~gilomaglioma~~, or prostate.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and SN-38 are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and SN-38 are administered to the mammal and the cancer is colon.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and temozolomide are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and temozolomide are administered to the mammal and the cancer is ~~gilomaglioma~~.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and a platinum agent are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and a platinum agent are administered to the mammal and the cancer is ovarian.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and GDC-0973 or a pharmaceutically acceptable salt thereof are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and GDC-0973 or a pharmaceutically acceptable salt thereof are administered to the mammal and the cancer is pancreatic, prostate, melanoma or breast.

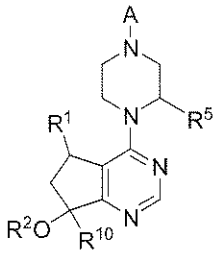
In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and PLX-4032 or a pharmaceutically acceptable salt thereof are administered to the mammal.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof and PLX-4032 or a pharmaceutically acceptable salt thereof are administered to the mammal and the cancer is melanoma.

In one specific aspect of the invention the compound of formula I or a pharmaceutically acceptable salt thereof is administered orally.

We claim:

1. Use of a compound of formula I:



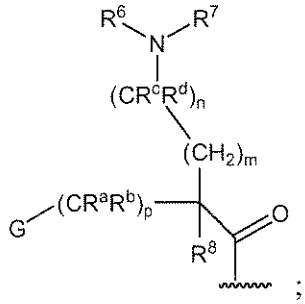
(I)

or a pharmaceutically acceptable salt thereof; wherein

R^1 is H, Me, Et, vinyl, CF_3, CHF_2 or CH_2F;

R^2 is H or Me;

R^5 is H, Me, Et, or CF_3;

A is  ;

G is phenyl optionally substituted by one to four R^9 groups or a 5-6 membered heteroaryl optionally substituted by a halogen;

R^6 and R^7 are independently H, OCH_3, (C_3-C_6 cycloalkyl)-(CH_2), (C_3-C_6 cycloalkyl)-(CH_2CH_2), V-$(CH_2)_{0-1}$ wherein V is a 5-6 membered heteroaryl having from one to two ring heteroatoms independently selected from N, O and S, W-$(CH_2)_{1-2}$ wherein W is phenyl optionally substituted with F, Cl, Br, I, OMe, CF_3 or Me, C_3-C_6-cycloalkyl optionally substituted with C_1-C_3 alkyl or O(C_1-C_3 alkyl), hydroxy-(C_3-C_6-cycloalkyl), fluoro-(C_3-C_6-cycloalkyl), $CH(CH_3)CH(OH)$phenyl, 4-6 membered heterocycle optionally substituted with F, OH, C_1-C_3-alkyl, cyclopropylmethyl or C(=O)(C_1-C_3 alkyl), or C_1-C_6-alkyl optionally substituted with one or more groups independently selected from OH, oxo, O(C_1-C_6-alkyl), CN, F, NH_2, NH(C_1-C_6-alkyl), N(C_1-C_6-alkyl)$_2$, cyclopropyl, phenyl, imidazolyl, piperidinyl, pyrrolidinyl, morpholinyl, tetrahydrofuranyl, oxetanyl, or tetrahydropyranyl,

or R^6 and R^7 together with the nitrogen to which they are attached form a 4-7 membered heterocyclic ring, wherein said heterocyclic ring is optionally substituted with one or more groups independently selected from OH, halogen, oxo, CF_3, CH_2CF_3, CH_2CH_2OH, O(C_1-C_3 alkyl), C(=O)CH_3, NH_2, NHMe, N(Me)$_2$, S(O)$_2CH_3$, cyclopropylmethyl and C_1-C_3 alkyl;

R^a and R^b are H,

or R^a is H, and R^b and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

R^c and R^d are H or Me,

or R^c and R^d together with the atom to which they are attached from a cyclopropyl ring;

R^8 is H, Me, F or OH,

or R^8 and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

each R^9 is independently halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, O-(C_1-C_6-alkyl), CF_3, OCF_3, S(C_1-C_6-alkyl), CN, OCH_2-phenyl, CH_2O-phenyl, NH_2, NH-(C_1-C_6-alkyl), N-(C_1-C_6-alkyl)$_2$, piperidine, pyrrolidine, CH_2F, CHF_2, OCH_2F, $OCHF_2$, OH, SO_2(C_1-C_6-alkyl), $C(O)NH_2$, C(O)NH(C_1-C_6-alkyl), and C(O)N(C_1-C_6-alkyl)$_2$;

R^{10} is H or Me; and

m, n and p are independently 0 or 1; and

one or more agents selected from 5-FU, capecitabine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for therapeutic treatment of a hyperproliferative disorder.

2. The use of claim 1, wherein compound of formula I or the salt thereof is administered simultaneously with the one or more agents.

3. The use of claim 1, wherein the compound of formula I or the salt thereof is administered sequentially with the one or more agents.

4. The use of claim 1, wherein the compound of formula I or the salt thereof and the one or more agents is administered separately.

5. The use of any one of claims 1-4 wherein the hyperproliferative disorder is cancer.

6. The use of claim 5 wherein the cancer is associated with PTEN mutation.

7. The use of claim 5 wherein the cancer is associated with AKT mutation, overexpression or amplification.

8. The use of claim 5 wherein the cancer is associated with PI3K mutation.

9. The use of claim 5 wherein the cancer is associated with Her2/ErbB2 mutation or amplification.

10. The use of any one of claims 5-9 wherein cancer is selected from, breast, lung, ovarian, prostate, melanoma, gastric, colon, renal, head and neck, and glioma.

11. The use of any one of claims 5-9 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and 5-FU are to be administered to the mammal.

12. The use of claim 11 wherein the cancer is breast cancer.

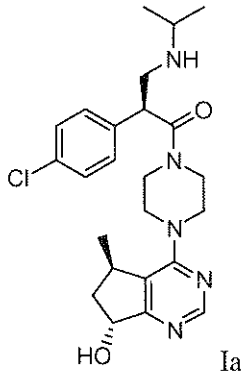
13. The use of claim 11 wherein further comprising administration of oxaliplatin to the mammal.

14. The use of claim 13 further comprising administration of leucovorin to the mammal.

15. The use of claim 13 or 14 wherein the cancer is gastric, ovarian, or colon.

16. The use of claim 13 or 14 wherein the cancer is gastric.

17. Use of a compound of formula Ia



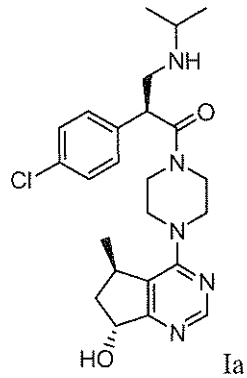
Ia

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a hyperproliferative disease in a mammal, wherein one or more agents selected from 5-FU, capecitabine, or a pharmaceutically acceptable salt thereof, are to be administered to the mammal.

18. The use of any one of claims 1-17 wherein the combination provides a synergistic effect in treating the hyperproliferative disorder.

19. The use of claim 18 wherein Combination Index value of the synergistic effect is less than about 0.8.

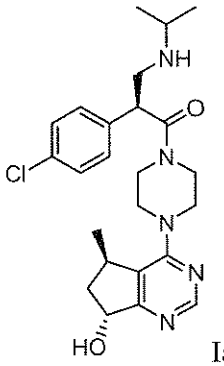
20. A compound of formula Ia



Ia

or a pharmaceutically acceptable salt thereof, for therapeutic use for improving the quality of life of a patient treated for a hyperproliferative disorder with an agent selected from 5-FU, capecitabine, or a pharmaceutically acceptable salt thereof.

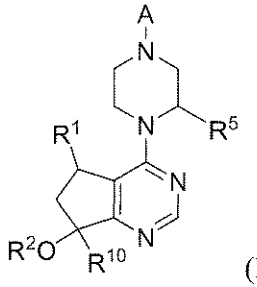
21. A compound of formula Ia



Ia,

or a pharmaceutically acceptable salt thereof, with an agent selected from 5-FU, capecitabine, or a pharmaceutically acceptable salt thereof.

22. The combination of a) a compound of formula I



(I)

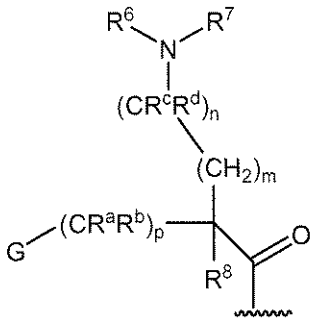
or a pharmaceutically acceptable salt thereof;

wherein

R^1 is H, Me, Et, vinyl, CF_3, CHF_2 or CH_2F;

R^2 is H or Me;

R^5 is H, Me, Et, or CF_3;

A is  ;

G is phenyl optionally substituted by one to four R^9 groups or a 5-6 membered heteroaryl

optionally substituted by a halogen;

R^6 and R^7 are independently H, OCH_3, (C_3-C_6 cycloalkyl)-(CH_2), (C_3-C_6 cycloalkyl)-(CH_2CH_2), V-$(CH_2)_{0-1}$ wherein V is a 5-6 membered heteroaryl having from one to two ring heteroatoms independently selected from N, O and S, W-$(CH_2)_{1-2}$ wherein W is phenyl optionally substituted with F, Cl, Br, I, OMe, CF_3 or Me, C_3-C_6-cycloalkyl optionally substituted with C_1-C_3 alkyl or O(C_1-C_3 alkyl), hydroxy-(C_3-C_6-cycloalkyl), fluoro-(C_3-C_6-cycloalkyl), $CH(CH_3)CH(OH)$phenyl, 4-6 membered heterocycle optionally substituted with F, OH, C_1-C_3-alkyl, cyclopropylmethyl or C(=O)(C_1-C_3 alkyl), or C_1-C_6-alkyl optionally substituted with one or more groups independently selected from OH, oxo, O(C_1-C_6-alkyl), CN, F, NH_2, NH(C_1-C_6-alkyl), N(C_1-C_6-alkyl)$_2$, cyclopropyl, phenyl, imidazolyl, piperidinyl, pyrrolidinyl, morpholinyl, tetrahydrofuranyl, oxetanyl, or tetrahydropyranyl,

or R^6 and R^7 together with the nitrogen to which they are attached form a 4-7 membered heterocyclic ring, wherein said heterocyclic ring is optionally substituted with one or more groups independently selected from OH, halogen, oxo, CF_3, CH_2CF_3, CH_2CH_2OH, O(C_1-C_3 alkyl), C(=O)CH_3, NH_2, NHMe, N(Me)$_2$, S(O)$_2CH_3$, cyclopropylmethyl and C_1-C_3 alkyl;

R^a and R^b are H,

or R^a is H, and R^b and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

R^c and R^d are H or Me,

or R^c and R^d together with the atom to which they are attached from a cyclopropyl ring;

R^8 is H, Me, F or OH,

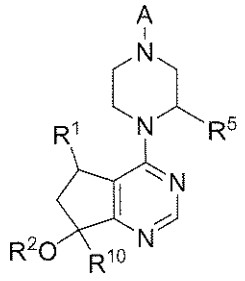
or R^8 and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

each R^9 is independently halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, O-(C_1-C_6-alkyl), CF_3, OCF_3, S(C_1-C_6-alkyl), CN, OCH_2-phenyl, CH_2O-phenyl, NH_2, NH-(C_1-C_6-alkyl), N-(C_1-C_6-alkyl)$_2$, piperidine, pyrrolidine, CH_2F, CHF_2, OCH_2F, $OCHF_2$, OH, SO_2(C_1-C_6-alkyl), C(O)NH_2, C(O)NH(C_1-C_6-alkyl), and C(O)N(C_1-C_6-alkyl)$_2$;

R^{10} is H or Me; and

m, n and p are independently 0 or 1; and b) one or more agents selected from 5-FU, capecitabine, or a pharmaceutically acceptable salt thereof.

23. A compound of formula I



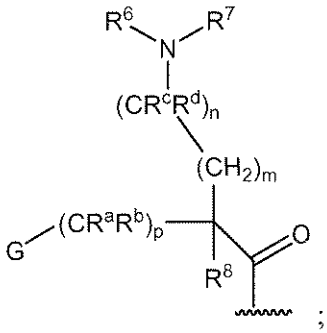
(I)

or a pharmaceutically acceptable salt thereof; wherein

R^1 is H, Me, Et, vinyl, CF_3, CHF_2 or CH_2F;

R^2 is H or Me;

R^5 is H, Me, Et, or CF_3;

A is  ;

G is phenyl optionally substituted by one to four R^9 groups or a 5-6 membered heteroaryl optionally substituted by a halogen;

R^6 and R^7 are independently H, OCH_3, (C_3-C_6 cycloalkyl)-(CH_2), (C_3-C_6 cycloalkyl)-(CH_2CH_2), V-$(CH_2)_{0\text{-}1}$ wherein V is a 5-6 membered heteroaryl having from one to two ring heteroatoms independently selected from N, O and S, W-$(CH_2)_{1\text{-}2}$ wherein W is phenyl optionally substituted with F, Cl, Br, I, OMe, CF_3 or Me, C_3-C_6-cycloalkyl optionally substituted with C_1-C_3 alkyl or O(C_1-C_3 alkyl), hydroxy-(C_3-C_6-cycloalkyl), fluoro-(C_3-C_6-cycloalkyl), $CH(CH_3)CH(OH)$phenyl, 4-6 membered heterocycle optionally substituted with F, OH, C_1-C_3-alkyl, cyclopropylmethyl or C(=O)(C_1-C_3 alkyl), or C_1-C_6-alkyl optionally substituted with one or more groups independently selected from OH, oxo, O(C_1-C_6-alkyl), CN, F, NH_2, NH(C_1-C_6-alkyl), N(C_1-C_6-alkyl)$_2$, cyclopropyl, phenyl, imidazolyl, piperidinyl, pyrrolidinyl, morpholinyl, tetrahydrofuranyl, oxetanyl, or tetrahydropyranyl,

or R^6 and R^7 together with the nitrogen to which they are attached form a 4-7 membered heterocyclic ring, wherein said heterocyclic ring is optionally substituted with one or more groups independently selected from OH, halogen, oxo, CF_3, CH_2CF_3, CH_2CH_2OH, O(C_1-C_3 alkyl), C(=O)CH_3, NH_2, NHMe, N(Me)$_2$, S(O)$_2CH_3$, cyclopropylmethyl and C_1-C_3 alkyl;

R^a and R^b are H,

or R^a is H, and R^b and R^6 together with the atoms to which they are attached form a 5-6

membered heterocyclic ring having one or two ring nitrogen atoms;

R^c and R^d are H or Me,

or R^c and R^d together with the atom to which they are attached from a cyclopropyl ring;

R^8 is H, Me, F or OH,

or R^8 and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

each R^9 is independently halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, O-(C_1-C_6-alkyl), CF_3, OCF_3, S(C_1-C_6-alkyl), CN, OCH_2-phenyl, CH_2O-phenyl, NH_2, NH-(C_1-C_6-alkyl), N-(C_1-C_6-alkyl)$_2$, piperidine, pyrrolidine, CH_2F, CHF_2, OCH_2F, $OCHF_2$, OH, SO_2(C_1-C_6-alkyl), C(O)NH_2, C(O)NH(C_1-C_6-alkyl), and C(O)N(C_1-C_6-alkyl)$_2$;

R^{10} is H or Me; and

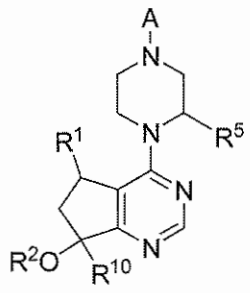
m, n and p are independently 0 or 1; for use in the treatment of a hyperproliferative disorder in a mammal, wherein one or more agents selected from 5-FU, capecitabine, or a pharmaceutically acceptable salt thereof are to be administered to the mammal.

24. A kit comprising a compound of formula I or a pharmaceutically acceptable salt thereof, a container, and a package insert or label indicating the administration of the compound of formula I with one or more agents selected from 5-FU, capecitabine, or a pharmaceutically acceptable salt thereof for treating a hyperproliferative disorder.

25. A system comprising a compound having formula I or a pharmaceutically acceptable salt thereof, and a chemotherapeutic agent selected from 5-FU, capecitabine or a pharmaceutically acceptable salt thereof; as a combined preparation for separate, simultaneous or sequential use in the treatment of a hyperproliferative disorder.

We claim:

1. A combination of, a) a compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib, or a pharmaceutically acceptable salt thereof, for the prophylactic or therapeutic treatment of a hyperproliferative disorder.

2. The combination of claim 1 wherein the hyperproliferative disorder is cancer.

3. The combination of claim 2 wherein the cancer is associated with PTEN mutation.

4. The combination of claim 2 wherein the cancer is associated with AKT mutation, overexpression or amplification.

5. The combination of claim 2 wherein the cancer is associated with PI3K mutation.

6. The combination of claim 2 wherein the cancer is associated with Her2/ErbB2 mutation or amplification.

7. The combination of any one of claims 2-6 wherein cancer is selected from, breast, lung, ovarian, prostate, melanoma, gastric, colon, renal, head and neck, and giloma.

8. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and 5-FU are to be administered to the mammal.

9. The combination of claim 8 wherein the cancer is breast cancer.

10. The combination of claim 8 wherein further comprising administration of oxaliplatin to the mammal.

11. The combination of claim 10 further comprising administration of folinic acid to the mammal.

12. The combination of claim 10 or 11 wherein the cancer is gastric, ovarian, or colon.

13. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and carboplatin are to be administered to the mammal.

14. The combination of claim 13 wherein the cancer is breast, lung, or prostate.

15. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and irinotecan are to be administered to the mammal.

16. The combination of claim 15 wherein the cancer is colon.

17. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and docetaxel are to be administered to the mammal.

18. The combination of claim 17 wherein the cancer is breast, giloma, lung, melanoma, ovarian, or prostate.

19. The combination of claim 17 wherein the cancer is breast, ovarian, or prostate.

20. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and doxorubicin are to be administered to the mammal.

21. The combination of claim 20 wherein the cancer is breast, lung, ovarian, giloma, or prostate.

22. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and SN-38 are to be administered to the mammal.

23. The combination of claim 22 wherein the cancer is colon.

24. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and temozolomide are to be administered to the mammal.

25. The combination of claim 24 wherein the cancer is giloma.

26. The combination of any one of claims 2-6 wherein the compound of formula I or the pharmaceutically acceptable salt thereof and a platinum agent are to be administered to the mammal.

27. The combination of claim 26 wherein the cancer is ovarian.

28. The combination of any one of claims 2-6 wherein temozolomide is to be administered.

29. The combination of any one of claims 2-6 wherein bevacizumab is to be administered.

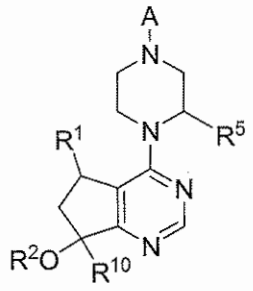
30. The combination of any one of claims 1-29 wherein the combination provides a synergistic effect in treating the hyperproliferative disorder.

31. The combination of claim 30 wherein Combination Index value of the synergistic effect is less than about 0.8.

32. A compound of formula Ia or a pharmaceutically acceptable salt thereof, as defined in claim 1 for therapeutic use for improving the quality of life of a patient treated for a hyperproliferative disorder with an agent selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib.

33. Use of a) a compound of formula I or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib in the manufacture of a medicament for treating a disease or condition modulated by AKT kinase in a mammal.

34. Use of a combination of, a) a compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib in the manufacture of a medicament for treating a hyperproliferative disorder in a mammal.

35. The combination of a) a compound of formula I or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib.

36. The use of a compound of formula I or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of a hyperproliferative disorder in a mammal, wherein one or more agents selected 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib are to be administered to the mammal.

37. The use of a compound of formula I or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of a disease or condition modulated by AKT kinase in a mammal, wherein one or more agents selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine,

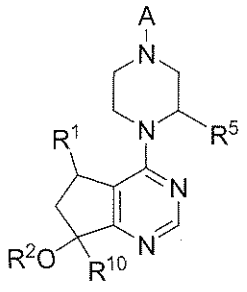
temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib are to be administered to the mammal.

38. A kit comprising a compound of formula I or a pharmaceutically acceptable salt thereof, a container, and a package insert or label indicating the administration of the compound of formula I with one or more agents selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib for treating a hyperproliferative disorder.

39. A system comprising a compound having formula I or a pharmaceutically acceptable salt thereof, and a chemotherapeutic agent selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib; as a combined preparation for separate, simultaneous or sequential use in the treatment of a hyperproliferative disorder.

ABSTRACT

The invention provides combinations comprising a) compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof wherein R^1, R^2, R^5, R^{10}, and A have any of the values defined in the specification ; and b) one or more agents selected from 5-FU, a platinum agent, leucovorin, irinotecan, docetaxel, doxorubicin, gemcitabine, SN-38, capecitabine, temozolomide, paclitaxel, bevacizumab, pertuzumab, tamoxifen, rapamycin and lapatinib. The combinations are particularly useful for treating hyperproliferative disorders, such as cancer.

[FIG. 1]