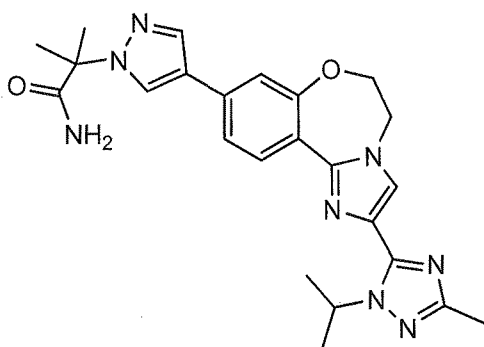


carbonate, calcium silicate, corn starch, magnesium carbonate, asbestos free talc, stearowet C, starch, starch 1500, magnesium lauryl sulfate, magnesium oxide, and combinations thereof.

19. The pharmaceutical formulation of claim 17 wherein GDC-0032 and the chemotherapeutic agent each comprise an amount from about 1 mg to about 1000 mg per unit dosage form.

20. The pharmaceutical formulation of claim 19 for use in a method of treatment of cancer.

21. The use of a therapeutic combination of GDC-0032 having the structure:



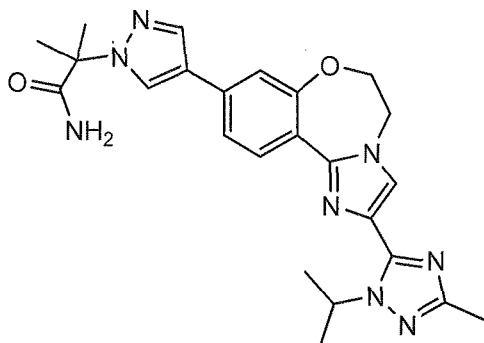
10 and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab in the manufacture of a medicament for the treatment of cancer selected from breast, cervical, colon, endometrial, glioma, lung, melanoma, ovarian, pancreatic, and prostate.

22. An article of manufacture for use in treating cancer selected from breast, cervical,
15 colon, endometrial, gastric, glioma, lung, melanoma, ovarian, pancreatic, and prostate
comprising:

- a) a combined formulation of any one of claims 1-16; and
- b) instructions for use.

24. A method for selecting compounds to be used in combination for the treatment of cancer comprising:

a) measuring a change in pAkt level in a tumour cell that had been administered a therapeutic combination of GDC-0032 having the structure



and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab; and

b) selecting a synergistic therapeutic combination which shows an increase in pAkt levels.

25. A use of a combination of GDC-0032 and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab in the manufacture of a medicament for the treatment of cancer selected from breast, cervical, colon, endometrial, gastric, glioma, lung, melanoma, ovarian, pancreatic, and prostate in a patient, wherein a biological sample obtained from the patient, prior to administration of the combination to the patient, has been tested for PIK3CA or PTEN mutation status, and wherein PIK3CA or PTEN mutation status is indicative of therapeutic responsiveness by the patient to the combination.

26. The use of claim ~~26~~ 25 wherein the patient is to be administered a therapeutically effective amount of the combination of GDC-0032 and a chemotherapeutic agent.

27. The use of claim 25 wherein the cancer is HER2 expressing breast cancer.

~~27~~28. The use of claim 25 wherein the cancer is estrogen receptor positive (ER+) breast cancer.

~~28~~29. The use of claim 25 wherein a biological sample has been tested by measuring functional PI3K protein level after administration of the combination of GDC-0032 and the
5 chemotherapeutic agent, wherein a change in the level of functional PI3K protein indicates that the patient will be resistant or responsive to the combination of GDC-0032 and a chemotherapeutic agent.

~~29~~30. The use of any one of claims 25-~~28~~29 wherein the GDC-0032 and the chemotherapeutic agent are to be administered to a mammal by alternation.

10 ~~30~~31. The use of claim ~~29~~30 wherein the mammal is to be administered the chemotherapeutic agent and subsequently to be administered GDC-0032.

~~31~~32. The use of claim ~~29~~30 wherein the GDC-0032 and the chemotherapeutic agent are to be administered by a dosing regimen where the GDC-0032 is to be administered in a range from twice daily to once every three weeks, and the chemotherapeutic agent is to be
15 administered in a range from twice daily to once every three weeks.

~~32~~33. The use of claim ~~31~~32 wherein the dosing regimen is repeated one or more times.

~~33~~34. The use of any one of claims 25-~~28~~29 wherein administration of the GDC-0032 and the chemotherapeutic agent results in a synergistic effect.

~~34~~35. The use of claim ~~33~~34 wherein administration of the GDC-0032 and the
20 chemotherapeutic agent results in a Combination Index value of less than about 0.7.

~~35~~36. The use of claim 25 wherein the cancer expresses a PIK3CA mutant selected from E542K, E545K, Q546R, H1047L and H1047R.

~~36~~37. The use of claim 25 wherein the cancer expresses a PTEN mutant.

~~37~~38. The use of claim 25 wherein the cancer is HER2 positive.

25 ~~38~~39. The use of claim 25 wherein the mammal is a breast cancer patient wherein the patient is HER2 negative, ER (estrogen receptor) negative, and PR (progesterone receptor) negative.

~~39~~40. The use of claim ~~38~~39 wherein the breast cancer subtype is Basal or Luminal.

4041. The use of claim ~~38~~39 wherein the patient is to be administered GDC-0032 and eribulin.

4142. The use of any one of claims ~~25-28~~29 wherein GDC-0032 and the chemotherapeutic agent are each to be administered in an amount from about 1 mg to about 1000
5 mg per unit dosage form.

4243. The use of any one of claims ~~25-28~~29 wherein GDC-0032 and the chemotherapeutic agent are to be administered in a ratio of about 1:50 to about 50:1 by weight.

4344. The use of any one of claims 25 to ~~28~~29 wherein the GDC-0032 and the chemotherapeutic agent are formulated in a single formulation for simultaneous administration
10 of the GDC-0032 and the chemotherapeutic agent, or in separate formulations for sequential administration of the GDC-0032 and the chemotherapeutic agent.

4445. A method of monitoring whether a patient with cancer selected from breast, cervical, colon, endometrial, gastric, glioma, lung, melanoma, ovarian, pancreatic, and prostate will respond to treatment with a combination of GDC-0032 and a chemotherapeutic agent, the
15 method comprising:

(a) detecting a PIK3CA or PTEN mutation in a biological sample obtained from the patient following administration of the at least one dose of the combination of GDC-0032 and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab; and

20 (b) comparing PIK3CA or PTEN mutation status in a biological sample obtained from the patient prior to administration of the combination of GDC-0032 and a chemotherapeutic agent to the patient,

wherein a change or modulation of PIK3CA or PTEN mutation status in the sample obtained following administration of the combination of GDC-0032 and a chemotherapeutic
25 agent identifies a patient who will respond to treatment with the combination of GDC-0032 and a chemotherapeutic agent.

4546. The method of claim ~~44~~45 wherein the cancer is HER2 expressing breast cancer.

4647. A method of optimizing therapeutic efficacy of the combination of GDC-0032 and a chemotherapeutic agent in the treatment of cancer selected from breast, cervical, colon, endometrial, gastric, glioma, lung, melanoma, ovarian, pancreatic, and prostate, the method comprising:

- 5 (a) detecting a PIK3CA or PTEN mutation in a biological sample obtained from a patient following administration of at least one dose of the combination of GDC-0032 and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab; and

(b) comparing the PIK3CA or PTEN status in a biological sample obtained from the patient prior to administration of the combination of GDC-0032 and a chemotherapeutic agent to the patient,

wherein a change or modulation of PIK3CA or PTEN in the sample obtained following
5 administration of the combination of GDC-0032 and a chemotherapeutic agent identifies a patient who has an increased likelihood of benefit from treatment with the combination of GDC-0032 and a chemotherapeutic agent.

~~47~~48. The method of claim ~~44~~45 wherein the cancer is HER2 expressing breast cancer.

~~48~~49. A method of identifying a biomarker for monitoring responsiveness to the
10 combination of GDC-0032 and a chemotherapeutic agent in the treatment of cancer selected from breast, cervical, colon, endometrial, gastric, glioma, lung, melanoma, ovarian, pancreatic, and prostate, the method comprising:

(a) detecting the expression, modulation, or activity of a biomarker selected from a PIK3CA or PTEN mutation in a biological sample obtained from a patient who has received at
15 least one dose of the combination of GDC-0032 and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab; and

(b) comparing the expression, modulation, or activity of the biomarker to the status of the biomarker in a reference sample wherein the reference sample is a biological sample
20 obtained from the patient prior to administration of the combination of GDC-0032 and a chemotherapeutic agent to the patient;

wherein the modulation of the biomarker changes by at least 2 fold lower or higher compared to the reference sample is identified as a biomarker useful for monitoring responsiveness to the combination of GDC-0032 and a chemotherapeutic agent.

25 ~~49~~50. The method of claim ~~48~~49 wherein the cancer is HER2 expressing breast cancer.

~~50~~51. A use of a combination of GDC-0032 and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-

0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab in the manufacture of a medicament for the treatment of cancer selected from breast, cervical, colon, endometrial, gastric, glioma, lung, melanoma, ovarian, pancreatic, and prostate in a patient, wherein treatment is based upon a sample from the patient having a PIK3CA or PTEN mutation.

5 ~~51~~52. The use of claim ~~50~~51 wherein the biomarker mutation is the H1047R or H1047L mutation of PIK3CA.

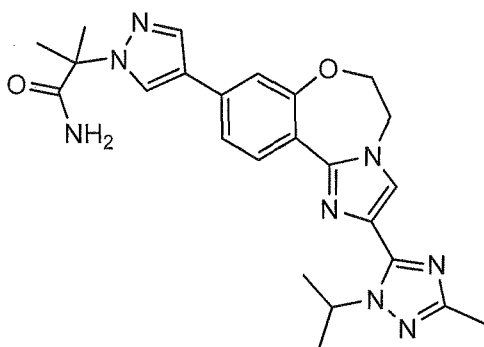
~~52~~53. The use of claim ~~50~~51 wherein the biomarker mutation is the E542K, E545K or Q546R mutation of PIK3CA.

~~53~~54. The use of claim ~~50~~51 wherein the cancer is HER2 expressing breast cancer.

10 ~~54~~55. The use of claim ~~50~~51 wherein the cancer is estrogen receptor positive (ER+) breast cancer.

~~55~~56. The use of any one of claims ~~50~~51 to ~~54~~55 wherein the GDC-0032 and the chemotherapeutic agent are formulated in a single formulation for simultaneous administration of the GDC-0032 and the chemotherapeutic agent, or in separate formulations for sequential
15 administration of the GDC-0032 and the chemotherapeutic agent.

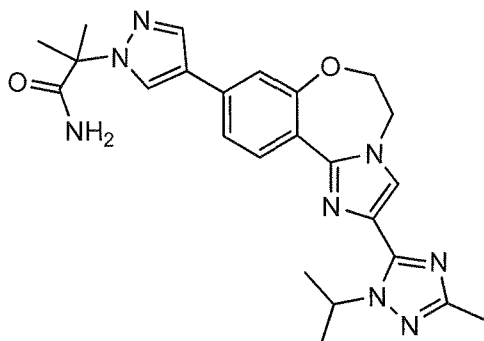
~~56~~57. A therapeutic combination of GDC-0032 having the structure:



and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab for use in the treatment of cancer selected from breast, cervical, colon, endometrial, glioma, lung, melanoma, ovarian, pancreatic, and prostate.

5758. The therapeutic combination of claim 5657 wherein the GDC-0032 and the chemotherapeutic agent are formulated in a single formulation for simultaneous administration of the GDC-0032 and the chemotherapeutic agent, or in separate formulations for sequential administration of the GDC-0032 and the chemotherapeutic agent.

5859. The use of a therapeutic combination of GDC-0032 having the structure:



and a chemotherapeutic agent selected from 5-FU, docetaxel, eribulin, gemcitabine, GDC-0973, GDC-0623, paclitaxel, fulvestrant, pertuzumab, trastuzumab emtansine, and trastuzumab in the manufacture of a medicament for the treatment of cancer selected from breast, cervical, colon, endometrial, glioma, lung, melanoma, ovarian, pancreatic, and prostate.

5960. The use of claim 5859, wherein the GDC-0032 and the chemotherapeutic agent are formulated in a single formulation for simultaneous administration of the GDC-0032 and the chemotherapeutic agent, or in separate formulations for sequential administration of the GDC-0032 and the chemotherapeutic agent.