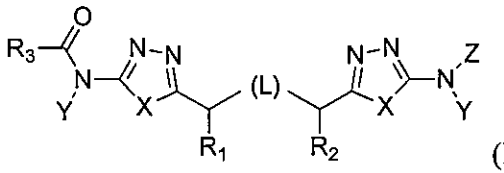
CLAIMS

1. Use of a compound of formula I, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of cancer



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H.

2. The use of claim 1, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2.

3. The use of claim 1, wherein L represents CH_2CH_2.

4. The use of any preceding claim, wherein Y represents H.

5. The use of any preceding claim, wherein X, independently for each occurrence, represents S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl.

6. The use of any preceding claim, wherein Z represents $R_3(CO)$.

7. The use of claim 6, wherein each occurrence of R_3 is not identical.

8. The use of any preceding claim, wherein R_1 and R_2 each represent H.

9. The use of any preceding claim, wherein R_3, independently for each occurrence, represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

10. The use of any preceding claim, wherein R_3, independently for each occurrence, represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, and R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl.

11. The use of claim 10, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, or heteroaryl.

12. The use of claim 10 or 11, wherein R_{10} represents hydroxy, hydroxyalkyl, or alkoxy.

13. The use of claim 1, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, and R_3, independently for each occurrence, represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

14. The use of claim 13, wherein each occurrence of R_3 is identical.

15. The use of claim 1, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, and R_3, independently for each occurrence, represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, and R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl.

16. The use of claim 15, wherein L represents CH_2CH_2.

17. The use of claim 15 or 16, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl or heteroaryl.

18. The use of claim 17, wherein R_8 represents substituted or unsubstituted aryl.

19. The use of any of claims 15-18, wherein R_{10} represents hydroxy, hydroxyalkyl or alkoxy.

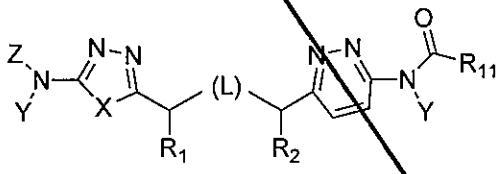
20. The use of claim 19, wherein R_{10} represents hydroxyalkyl.

21. The use of any one of claims 15-20, wherein each occurrence of R_3 is identical.

22. The use of claim 1, wherein L represents CH_2CH_2, Y represents H, X, independently for each occurrence, represents S or CH=CH, Z represents $R_3(CO)$, R_1 and R_2 each represent H, and R_3, independently for each occurrence, represents arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

23. The use of claim 22, wherein each occurrence of R_3 is identical.

24. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of cancer



(Ia),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl.

25. The use of claim 24, wherein R_{11} represents substituted or unsubstituted arylalkyl.

26. The use of claim 25, wherein R_{11} represents substituted or unsubstituted benzyl.

27. The use of any of claims 24-26, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2.

28. The use of claim 27, wherein L represents CH_2CH_2.

29. The use of any of claims 24-28, wherein each Y represents H.

30. The use of any of claims 24-29, wherein X represents S or CH=CH.

31. The use of claim 30, wherein X represents S.

32. The use of any of claims 24-31, wherein Z represents $R_3(CO)$.

33. The use of claim 32, wherein R_3 and R_{11} are not identical.

34. The use of any of claims 24-33, wherein R_1 and R_2 each represent H.

35. The use of claim 32, wherein R_3 represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

36. The use of claim 35, wherein R_3 represents substituted or unsubstituted heteroarylalkyl.

37. The use of claim 32, wherein R_3 represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, and R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl.

38. The use of claim 37, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, or heteroaryl.

39. The use of claim 37 or 38, wherein R_{10} represents hydroxy, hydroxyalkyl, or alkoxy.

40. The use of claim 24, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl, and R_{11} represents substituted or unsubstituted arylalkyl.

41. The use of claim 40, wherein R_3 represents substituted or unsubstituted heteroarylalkyl.

42. The use of claim 24, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl, and R_{11} represents substituted or unsubstituted arylalkyl.

43. The use of claim 42, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl or heteroaryl.

44. The use of claim 43, wherein R_8 represents heteroaryl.

45. The use of any of claims 42-44, wherein R_{10} represents hydroxy, hydroxyalkyl or alkoxy.

46. The use of claim 24, wherein L represents CH_2CH_2, Y represents H, X represents S or CH=CH, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl, and R_{11} represents substituted or unsubstituted arylalkyl.

47. The use of claim 46, wherein R_3 represents substituted or unsubstituted heteroarylalkyl.

48. The use of claim 24, wherein L represents CH_2CH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl or heteroaryl, R_9 represents H, R_{10} represents hydroxy, hydroxyalkyl or alkoxy, and R_{11} represents substituted or unsubstituted arylalkyl.

49. The use of any preceding claim, wherein the cancer is selected from breast cancer, colorectal cancer, endocrine cancer, lung cancer, melanoma, mesothelioma, renal cancer and a B cell malignancy.

50. The use of claim 49, wherein the cancer is breast cancer.

51. The use of claim 50, wherein the breast cancer comprises basal-type breast cancer cells, triple-negative breast cancer cells or claudin-low breast cancer cells.

52. The use of claim 51, wherein the breast cancer comprises basal-type breast cancer cells.

53. The use of claim 51, wherein the breast cancer comprises triple-negative breast cancer cells.

54. The use of claim 51, wherein the breast cancer comprises claudin-low breast cancer cells.

55. The use of claim 49, wherein the cancer is colorectal cancer.

56. The use of claim 49, wherein the cancer is endocrine cancer.

57. The use of claim 56, wherein the endocrine cancer is selected from adrenal cortex adenoma, adrenal cortex carcicnoma, adrenal gland pheochromocytoma and parathyroid gland adenoma.

58. The use of claim 49, wherein the cancer is melanoma.

59. The use of claim 49, wherein the cancer is renal cancer.

60. The use of claim 49, wherein the cancer is a B cell malignancy.

61. The use of claim 60, wherein the B cell malignancy is selected from multiple myeloma, leukemia and lymphoma.

62. The use of claim 61, wherein the B cell malignancy is multiple myeloma.

63. The use of claim 61, wherein the B cell malignancy is leukemia.

64. The use of claim 63, wherein the leukemia is selected from acute lymphoblastic leukemia and chronic lymphoblastic leukemia.

65. The use of claim 61, wherein the B cell malignancy is lymphoma.

66. The use of claim 65, wherein the lymphoma is selected from Burkitt's lymphoma, Diffuse large B cell lymphoma, follicular lymphoma and Hodgkin's lymphoma.

67. The use of any preceding claim, further comprising conjointly administering one or more additional chemotherapeutic agents.

68. The use of claim 67, wherein conjointly administering one or more additional chemotherapeutic agents provide improved efficacy relative to each individual administration of the compound of formula I or the one or more additional chemotherapeutic agent.

69. The use of claim 68, wherein conjointly administering one or more additional chemotherapeutic agents provide a synergistic effect.

70. The use of claim 69, wherein conjointly administering one or more additional chemotherapeutic agents provide an additive effect.

71. The use of any of claims 67-70, wherein the compound of formula I and the one or more additional chemotherapeutic agents are administered simultaneously.

72. The use of any of claims 67-70, wherein the one or more additional chemotherapeutic agents are administered within about 5 minutes to within about 168 hours prior to or after administration of the compound of formula I.

73. The use of any of claims 67-72, wherein the one or more additional chemotherapeutic agents are selected from ABT-263, aminoglutethimide, amsacrine, anastrozole, asparaginase, bcg, bicalutamide, bleomycin, bortezomib, buserelin, busulfan, campothecin, capecitabine, carboplatin, carfilzomib, carmustine, chlorambucil, chloroquine, cisplatin, cladribine, clodronate, colchicine, cyclophosphamide, cyproterone, cytarabine, dacarbazine, dactinomycin, daunorubicin, demethoxyviridin, dexamethasone, dichloroacetate, dienestrol, diethylstilbestrol, docetaxel, doxorubicin, epirubicin, estradiol, estramustine, etoposide, everolimus, exemestane, filgrastim, fludarabine, fludrocortisone, fluorouracil and 5-fluorouracil, fluoxymesterone, flutamide, gemcitabine, genistein, goserelin, hydroxyurea, idarubicin, ifosfamide, imatinib, interferon, irinotecan, ironotecan, lenalidomide, letrozole, leucovorin, leuprolide, levamisole, lomustine, lonidamine, mechlorethamine, medroxyprogesterone, megestrol, melphalan, mercaptopurine, mesna, metformin, methotrexate, mitomycin, mitotane, mitoxantrone, nilutamide, nocodazole, octreotide, oxaliplatin, paclitaxel, pamidronate, pentostatin, perifosine, PF-04691502, plicamycin, pomalidomide, porfimer, procarbazine, raltitrexed, rituximab, romidepsin, sorafenib, streptozocin, sunitinib, suramin, tamoxifen, temozolomide, temsirolimus, teniposide, testosterone, thalidomide, thioguanine, thiotepa, titanocene dichloride, topotecan, trastuzumab, tretinoin, vinblastine, vincristine, vindesine, vinorelbine, and vorinostat (SAHA).

74. The use of claim 73, wherein the one or more additional chemotherapeutic agents are selected from bortezomib, capecitabine, carboplatin, carfilzomib, cyclophosphamide, daunorubicin, dexamethasone, docetaxel, doxorubicin, epirubicin, eribulin, fluorouracil, gemcitabine, ixabepilone, lenalidomide, methotrexate, mitoxantrone, mutamycin, paclitaxel, pomalidomide, rituximab, thalidomide, thiotepa, vincristine, and vinorelbine.

75. The use of claim 74, wherein the one or more additional chemotherapeutic agents are selected from bortezomib, carfilzomib, dexamethasone, doxorubicin, lenalidomide, pacilitaxel, pomalidomide, thalidomide, and rituximab.

76. An in-vitro method of identifying a cancer patient that may benefit from treatment with a glutaminase inhibitor comprising determining the ratio of glutamate to glutamine in cancer cells of the cancer patient, wherein a ratio greater than or equal to 1.5 indicates the patient may benefit from treatment with a glutaminase inhibitor.

77. The method of claim 76, wherein the ratio is greater than or equal to 2.0.

78. The method of claim 76 or 77, wherein the method of determining the ratio includes measuring levels of glutamate and glutamine in the cancer cells of the cancer patient.

79. The method of any of claims 76-78, wherein the cancer is selected from a B cell malignancy, breast cancer, colorectal cancer, endocrine cancer, lung cancer, melanoma, mesothelioma and renal cancer.

80. The method of claim 79, wherein the cancer is breast cancer.

81. The method of claim 80, wherein the breast cancer comprises basal-type breast cancer cells, triple-negative breast cancer cells or claudin-low breast cancer cells.

82. The method of claim 81, wherein the breast cancer comprises basal-type breast cancer cells.

83. The method of claim 81, wherein the breast cancer comprises triple-negative breast cancer cells.

84. The method of claim 81, wherein the breast cancer comprises claudin-low breast cancer cells.

85. The method of claim 79, wherein the cancer is colorectal cancer.

86. The method of claim 79, wherein the cancer is endocrine cancer.

87. The method of claim 86, wherein the endocrine cancer is selected from adrenal cortex adenoma, adrenal cortex carcicnoma, adrenal gland pheochromocytoma and parathyroid gland adenoma.

88. The method of claim 79, wherein the cancer is melanoma.

89. The method of claim 79, wherein the cancer is renal cancer.

90. The method of claim 79, wherein the cancer is a B cell malignancy.

91. The method of claim 90, wherein the B cell malignancy is selected from multiple myeloma, leukemia and lymphoma.

92. The method of claim 91, wherein the B cell malignancy is multiple myeloma.

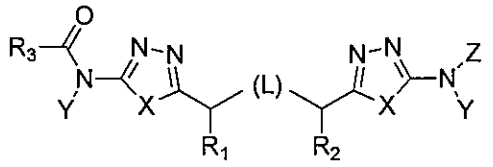
93. The method of claim 91, wherein the B cell malignancy is leukemia.

94. The method of claim 93, wherein the leukemia is selected from acute lymphoblastic leukemia and chronic lymphoblastic leukemia.

95. The method of claim 91, wherein the B cell malignancy is lymphoma.

96. The method of claim 95, wherein the lymphoma is selected from Burkitt's lymphoma, Diffuse large B cell lymphoma, follicular lymphoma and Hodgkin's lymphoma.

97. Use of a compound of formula I, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a cancer patient,



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

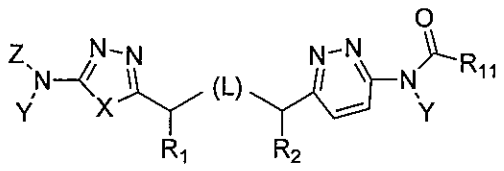
R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H,

wherein 1) the ratio of glutamate to glutamine in cancer cells of the cancer patient is determined; and 2) the medicament is administered if the ratio of glutamate to glutamine is greater than or equal to 1.5.

98. The use of claim 97, wherein the compound is a compound as described in any of claims 2-23.

99. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a cancer patient,



(Ia),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy,

aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl

wherein 1) the ratio of glutamate to glutamine in cancer cells of the cancer patient is determined; and 2) the medicament is administered if the ratio of glutamate to glutamine is greater than or equal to 1.5.

100. The use of claim 99, wherein the compound is a compound as described in any of claims 25-48.

101. The use of any of claims 97-100, wherein the ratio is greater than or equal to 2.0.

102. The use of any of claims 97-101, wherein the method of determining the ratio includes measuring levels of glutamate and glutamine in the cancer cells of the cancer patient.

103. The use of any of claims 97-102, wherein the cancer is selected from a B cell malignancy, breast cancer, colorectal cancer, endocrine cancer, lung cancer, melanoma, mesothelioma and renal cancer.

104. The use of claim 103, wherein the cancer is breast cancer.

105. The use of claim 104, wherein the breast cancer comprises basal-type breast cancer cells, triple-negative breast cancer cells or claudin-low breast cancer cells.

106. The use of claim 105, wherein the breast cancer comprises basal-type breast cancer cells.

107. The use of claim 105, wherein the breast cancer comprises triple-negative breast cancer cells.

108. The use of claim 105, wherein the breast cancer comprises claudin-low breast cancer cells.

109. The use of claim 103, wherein the cancer is colorectal cancer.

110. The use of claim 103, wherein the cancer is endocrine cancer.

111. The use of claim 110, wherein the endocrine cancer is selected from adrenal cortex adenoma, adrenal cortex carcicnoma, adrenal gland pheochromocytoma and parathyroid gland adenoma.

112. The use of claim 103, wherein the cancer is melanoma.

113. The use of claim 103, wherein the cancer is renal cancer.

114. The use of claim 103, wherein the cancer is a B cell malignancy.

115. The use of claim 114, wherein the B cell malignancy is selected from multiple myeloma, leukemia and lymphoma.

116. The use of claim 115, wherein the B cell malignancy is multiple myeloma.

117. The use of claim 115, wherein the B cell malignancy is leukemia.

118. The use of claim 117, wherein the leukemia is selected from acute lymphoblastic leukemia and chronic lymphoblastic leukemia.

119. The use of claim 115, wherein the B cell malignancy is lymphoma.

120. The use of claim 119, wherein the lymphoma is selected from Burkitt's lymphoma, Diffuse large B cell lymphoma, follicular lymphoma and Hodgkin's lymphoma.

121. An in-vitro method of identifying a cancer patient that may benefit from treatment with a glutaminase inhibitor, comprising determining the ratio of GLS:GS ratio in cancer cells of the cancer patient, wherein a ratio greater than or equal to 0.05 indicates the patient may benefit from treatment with a glutaminase inhibitor.

122. The method of claim 121, wherein the ratio is greater than or equal to 1.

123. The method of claim 121 or 122, wherein the method of determining the ratio comprises measuring levels of GLS and GS in the cancer cells of the cancer patient.

124. The method of claim 123, wherein measuring the levels of GLS and GS comprises measuring mRNA amounts.

125. The method of claim 123, wherein measuring the levels of GLS and GS comprises measuring protein amounts.

126. The method of any one of claims 121-125, wherein GLS is GAC.

127. The method of any one of claims 121-125, wherein GLS is KGA.

128. The method of any one of claims 121-125, wherein GLS is both GAC and KGA.

129. The method of any of claims 121-128, wherein the cancer is selected from a B cell malignancy, breast cancer, colorectal cancer, endocrine cancer, lung cancer, melanoma, mesothelioma and renal cancer.

130. The method of claim 129, wherein the cancer is breast cancer.

131. The method of claim 130, wherein the breast cancer comprises basal-type breast cancer cells, triple-negative breast cancer cells or claudin-low breast cancer cells.

132. The method of claim 130, wherein the breast cancer comprises basal-type breast cancer cells.

133. The method of claim 130, wherein the breast cancer comprises triple-negative breast cancer cells.

134. The method of claim 130, wherein the breast cancer comprises claudin-low breast cancer cells.

135. The method of claim 129, wherein the cancer is colorectal cancer.

136. The method of claim 129, wherein the cancer is endocrine cancer.

137. The method of claim 136, wherein the endocrine cancer is selected from adrenal cortex adenoma, adrenal cortex carcicnoma, adrenal gland pheochromocytoma and parathyroid gland adenoma.

138. The method of claim 129, wherein the cancer is melanoma.

139. The method of claim 129, wherein the cancer is renal cancer.

140. The method of claim 129, wherein the cancer is a B cell malignancy.

141. The method of claim 140, wherein the B cell malignancy is selected from multiple myeloma, leukemia and lymphoma.

142. The method of claim 140, wherein the B cell malignancy is multiple myeloma.

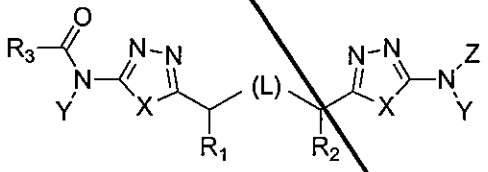
143. The method of claim 140, wherein the B cell malignancy is leukemia.

144. The method of claim 143, wherein the leukemia is selected from acute lymphoblastic leukemia and chronic lymphoblastic leukemia.

145. The method of claim 140, wherein the B cell malignancy is lymphoma.

146. The method of claim 145, wherein the lymphoma is selected from Burkitt's lymphoma, Diffuse large B cell lymphoma, follicular lymphoma and Hodgkin's lymphoma.

147. Use of a compound of formula I, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a cancer patient,



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H

wherein 1) the ratio of GLS to GS in cancer cells of the cancer patient is determined; and 2) the medicament is administered if the ratio of GSL to GS is greater than or equal to 0.05,.

148. The use of claim 147, wherein the compound is a compound as described in any of claims 2-23.

149. The use of claim 147, wherein the ratio is greater than or equal to 1.

150. The use of claim 147 or 149, wherein the method of determining the ratio comprises measuring the levels of GLS and GS in the cancer cells of the cancer patient.

151. The use of claim 150, wherein measuring the levels of GLS and GS comprises measuring mRNA amounts.

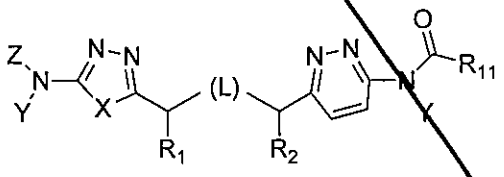
152. The use of claim 151, wherein measuring the levels of GLS and GS comprises measuring protein amounts.

153. The use of any one of claims 147-152, wherein GLS is GAC.

154. The use of any one of claims 147-152, wherein GLS is KGA.

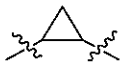
155. The use of any one of claims 147-152, wherein GLS is both GAC and KGA.

156. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a cancer patient,



(Ia),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

X, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl,

wherein 1) the ratio of GLS to GS in cancer cells of the cancer patient is determined; and 2) the medicament is administered if the ratio of GLS to GS is greater than or equal to 0.05.

157. The use of claim 156, wherein the compound is a compound as described in any of claims 25-48.

158. The use of claim 156 or 157, wherein the ratio is greater than or equal to 1.

159. The use of any one of claims 156-158, wherein the method of determining the ratio comprises measuring the levels of GLS and GS in the cancer cells of the cancer patient.

160. The use of claim 159, wherein measuring the levels of GLS and GS comprises measuring mRNA amounts.

161. The use of claim 159, wherein measuring the levels of GLS and GS comprises measuring protein amounts.

162. The use of any one of claims 156-161, wherein GLS is GAC.

163. The use of any one of claims 156-161, wherein GLS is KGA.

164. The use of any one of claims 156-161, wherein GLS is both GAC and KGA.

165. The use of any of claims 156-164, wherein the cancer is selected from a B cell malignancy, breast cancer, colorectal cancer, endocrine cancer, lung cancer, melanoma, mesothelioma and renal cancer.

166. The use of claim 165, wherein the cancer is breast cancer.

167. The use of claim 166, wherein the breast cancer comprises basal-type breast cancer cells, triple-negative breast cancer cells or claudin-low breast cancer cells.

168. The use of claim 166, wherein the breast cancer comprises basal-type breast cancer cells.

169. The use of claim 166, wherein the breast cancer comprises triple-negative breast cancer cells.

170. The use of claim 166, wherein the breast cancer comprises claudin-low breast cancer cells.

171. The use of claim 165, wherein the cancer is colorectal cancer.

172. The use of claim 165, wherein the cancer is endocrine cancer.

173. The use of claim 172, wherein the endocrine cancer is selected from adrenal cortex adenoma, adrenal cortex carcicnoma, adrenal gland pheochromocytoma and parathyroid gland adenoma.

174. The use of claim 165, wherein the cancer is melanoma.

175. The use of claim 165, wherein the cancer is renal cancer.

176. The use of claim 165, wherein the cancer is a B cell malignancy.

177. The use of claim 176, wherein the B cell malignancy is selected from multiple myeloma, leukemia and lymphoma.

178. The use of claim 176, wherein the B cell malignancy is multiple myeloma.

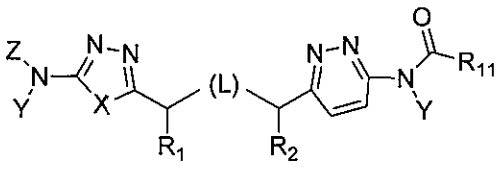
179. The use of claim 176, wherein the B cell malignancy is leukemia.

180. The use of claim 179, wherein the leukemia is selected from acute lymphoblastic leukemia and chronic lymphoblastic leukemia.

181. The use of claim 176, wherein the B cell malignancy is lymphoma.

182. The use of claim 181, wherein the lymphoma is selected from Burkitt's lymphoma, Diffuse large B cell lymphoma, follicular lymphoma and Hodgkin's lymphoma.

183. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a cancer patient


(Ia),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

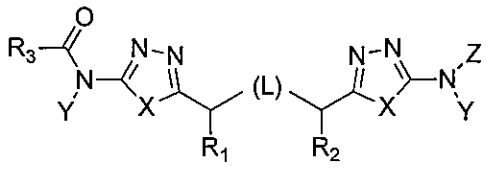
R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl,

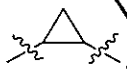
wherein 1) glutaminase activity in cancer cells of the cancer patient is determined; and 2) the medicament is administered if the activity is greater than or equal to 0.005 μmol/min/mg of protein,.

184. Use of a compound of formula I, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a cancer patient



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

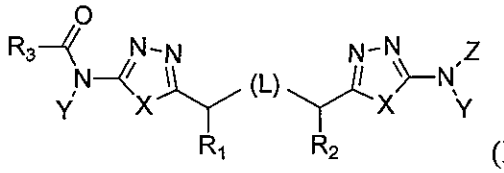
heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H,

wherein 1) glutaminase activity in cancer cells of the cancer patient is determined; and 2) the medicament is administered if the activity is greater than or equal to 0.005 μmol/min/mg of protein.

CLAIMS

1. Use of a compound of formula I, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of cancer,



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

wherein the cancer is claudin-low breast cancer.

2. The use of claim 1, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2.

3. The use of claim 1, wherein L represents CH_2CH_2.

4. The use of any preceding claim, wherein Y represents H.

5. The use of any preceding claim, wherein X, independently for each occurrence, represents S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl.

6. The use of any preceding claim, wherein Z represents $R_3(CO)$.

7. The use of claim 6, wherein each occurrence of R_3 is not identical.

8. The use of any preceding claim, wherein R_1 and R_2 each represent H.

9. The use of any preceding claim, wherein R_3, independently for each occurrence, represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

10. The use of any preceding claim, wherein R_3, independently for each occurrence, represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, and R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl.

11. The use of claim 10, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, or heteroaryl.

12. The use of claim 10 or 11, wherein R_{10} represents hydroxy, hydroxyalkyl, or alkoxy.

13. The use of claim 1, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, and R_3, independently for each occurrence, represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

14. The use of claim 13, wherein each occurrence of R_3 is identical.

15. The use of claim 1, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, and R_3, independently for each occurrence, represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, and R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl.

16. The use of claim 15, wherein L represents CH_2CH_2.

17. The use of claim 15 or 16, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl or heteroaryl.

18. The use of claim 17, wherein R_8 represents substituted or unsubstituted aryl.

19. The use of any of claims 15-18, wherein R_{10} represents hydroxy, hydroxyalkyl or alkoxy.

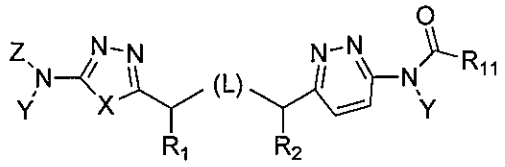
20. The use of claim 19, wherein R_{10} represents hydroxyalkyl.

21. The use of any one of claims 15-20, wherein each occurrence of R_3 is identical.

22. The use of claim 1, wherein L represents CH_2CH_2, Y represents H, X, independently for each occurrence, represents S or CH=CH, Z represents $R_3(CO)$, R_1 and R_2 each represent H, and R_3, independently for each occurrence, represents arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

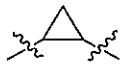
23. The use of claim 22, wherein each occurrence of R_3 is identical.

24. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of cancer,



(Ia),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl;

wherein the cancer is claudin-low breast cancer.

25. The use of claim 24, wherein R_{11} represents substituted or unsubstituted arylalkyl.

26. The use of claim 25, wherein R_{11} represents substituted or unsubstituted benzyl.

27. The use of claim any of claims 24-26, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2.

28. The use of claim 27, wherein L represents CH_2CH_2.

29. The use of any of claims 24-28, wherein each Y represents H.

30. The use of any of claims 24-29, wherein X represents S or CH=CH.

31. The use of claim 30, wherein X represents S.

32. The use of any of claims 24-31, wherein Z represents $R_3(CO)$.

33. The use of claim 32, wherein R_3 and R_{11} are not identical.

34. The use of any of claims 24-33, wherein R_1 and R_2 each represent H.

35. The use of claim 32, wherein R_3 represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.

36. The use of claim 35, wherein R_3 represents substituted or unsubstituted heteroarylalkyl.

37. The use of claim 32, wherein R_3 represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, and R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl.

38. The use of claim 37, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, or heteroaryl.

39. The use of claim 37 or 38, wherein R_{10} represents hydroxy, hydroxyalkyl, or alkoxy.

40. The use of claim 24, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl, and R_{11} represents substituted or unsubstituted arylalkyl.

41. The use of claim 40, wherein R_3 represents substituted or unsubstituted heteroarylalkyl.

42. The use of claim 24, wherein L represents CH_2SCH_2, CH_2CH_2, CH_2S or SCH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl, heteroaryl or heteroaralkyl, R_9 represents H, R_{10} represents hydroxy, hydroxyalkyl, alkoxy or alkoxyalkyl, and R_{11} represents substituted or unsubstituted arylalkyl.

43. The use of claim 42, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl or heteroaryl.

44. The use of claim 43, wherein R_8 represents heteroaryl.

45. The use of any of claims 42-44, wherein R_{10} represents hydroxy, hydroxyalkyl or alkoxy.

46. The use of claim 24, wherein L represents CH_2CH_2, Y represents H, X represents S or CH=CH, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents substituted or

unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl, and R_{11} represents substituted or unsubstituted arylalkyl.

47. The use of claim 46, wherein R_3 represents substituted or unsubstituted heteroarylalkyl.

48. The use of claim 24, wherein L represents CH_2CH_2, Y represents H, X represents S, Z represents $R_3(CO)$, R_1 and R_2 each represent H, R_3 represents $C(R_8)(R_9)(R_{10})$, wherein R_8 represents substituted or unsubstituted aryl, arylalkyl or heteroaryl, R_9 represents H, R_{10} represents hydroxy, hydroxyalkyl or alkoxy, and R_{11} represents substituted or unsubstituted arylalkyl.

49. The use of any preceding claim, wherein the medicament is conjointly administered with one or more additional chemotherapeutic agents.

50. The use of claim 49, wherein conjoint administration of one or more additional chemotherapeutic agents provides improved efficacy relative to each individual administration of the compound of formula I or the one or more additional chemotherapeutic agents.

51. The use of claim 50, wherein conjoint administration of one or more additional chemotherapeutic agents provides a synergistic effect.

52. The use of claim 51, wherein conjoint administration of one or more additional chemotherapeutic agents provides an additive effect.

53. The use of any of claims 49-52, wherein the compound of formula I and the one or more additional chemotherapeutic agents are administered simultaneously.

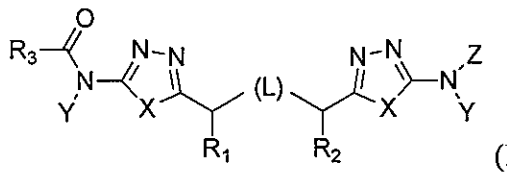
54. The use of any of claims 49-52, wherein the one or more additional chemotherapeutic agents are administered within about 5 minutes to within about 168 hours prior to or after administration of the compound of formula I.

55. The use of any of claims 49-54, wherein the one or more additional chemotherapeutic agents are selected from ABT-263, aminoglutethimide, amsacrine, anastrozole, asparaginase, bcg, bicalutamide, bleomycin, bortezomib, buserelin, busulfan, campothecin, capecitabine, carboplatin, carfilzomib, carmustine, chlorambucil, chloroquine, cisplatin, cladribine, clodronate, colchicine, cyclophosphamide, cyproterone, cytarabine, dacarbazine, dactinomycin, daunorubicin, demethoxyviridin, dexamethasone, dichloroacetate, dienestrol, diethylstilbestrol, docetaxel, doxorubicin, epirubicin, estradiol, estramustine, etoposide, everolimus, exemestane, filgrastim, fludarabine, fludrocortisone, fluorouracil and 5-fluorouracil, fluoxymesterone, flutamide, gemcitabine, genistein, goserelin, hydroxyurea, idarubicin, ifosfamide, imatinib, interferon, irinotecan, ironotecan, lenalidomide, letrozole, leucovorin, leuprolide, levamisole, lomustine, lonidamine, mechlorethamine, medroxyprogesterone, megestrol, melphalan, mercaptopurine, mesna, metformin, methotrexate, mitomycin, mitotane, mitoxantrone, nilutamide, nocodazole, octreotide, oxaliplatin, paclitaxel, pamidronate, pentostatin, perifosine, PF-04691502, plicamycin, pomalidomide, porfimer, procarbazine, raltitrexed, rituximab, romidepsin, sorafenib, streptozocin, sunitinib, suramin, tamoxifen, temozolomide, temsirolimus, teniposide, testosterone, thalidomide, thioguanine, thiotepa, titanocene dichloride, topotecan, trastuzumab, tretinoin, vinblastine, vincristine, vindesine, vinorelbine, and vorinostat (SAHA).

56. The use of claim 55, wherein the one or more additional chemotherapeutic agents are selected from bortezomib, capecitabine, carboplatin, carfilzomib, cyclophosphamide, daunorubicin, dexamethasone, docetaxel, doxorubicin, epirubicin, eribulin, fluorouracil, gemcitabine, ixabepilone, lenalidomide, methotrexate, mitoxantrone, mutamycin, paclitaxel, pomalidomide, rituximab, thalidomide, thiotepa, vincristine, and vinorelbine.

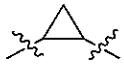
57. The use of claim 56, wherein the one or more additional chemotherapeutic agents are selected from bortezomib, carfilzomib, dexamethasone, doxorubicin, lenalidomide, pacilitaxel, pomalidomide, thalidomide, and rituximab.

58. Use of a compound of formula I, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer,



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

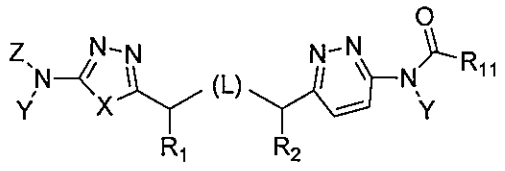
heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

wherein 1) the ratio of glutamate to glutamine in cells of the cancer is determined; and 2) the medicament is administered if the ratio of glutamate to glutamine is greater than or equal to 1.5.

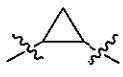
59. The use of claim 58, wherein the compound is a compound as described in any of claims 2-23.

60. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer,



(Ia),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl;

wherein 1) the ratio of glutamate to glutamine in cells of the cancer is determined; and 2) the medicament is administered if the ratio of glutamate to glutamine is greater than or equal to 1.5.

61. The use of claim 60, wherein the compound is a compound as described in any of claims 25-48.

62. The use of any of claims 58-61, wherein the ratio is greater than or equal to 2.0.

63. The use of any of claims 58-62, wherein the ratio is determined by measuring levels of glutamate and glutamine in the cancer cells.

64. The use of any of claims 58-63, wherein the cancer is selected from a B cell malignancy, breast cancer, colorectal cancer, endocrine cancer, lung cancer, melanoma, mesothelioma and renal cancer.

65. The use of claim 64, wherein the cancer is breast cancer.

66. The use of claim 65, wherein the breast cancer comprises basal-type breast cancer cells, triple-negative breast cancer cells or claudin-low breast cancer cells.

67. The use of claim 66, wherein the breast cancer comprises basal-type breast cancer cells.

68. The use of claim 66, wherein the breast cancer comprises triple-negative breast cancer cells.

69. The use of claim 66, wherein the breast cancer comprises claudin-low breast cancer cells.

70. The use of claim 64, wherein the cancer is colorectal cancer.

71. The use of claim 64, wherein the cancer is endocrine cancer.

72. The use of claim 71, wherein the endocrine cancer is selected from adrenal cortex adenoma, adrenal cortex carcicnoma, adrenal gland pheochromocytoma and parathyroid gland adenoma.

73. The use of claim 64, wherein the cancer is melanoma.

74. The use of claim 64, wherein the cancer is renal cancer.

75. The use of claim 64, wherein the cancer is a B cell malignancy.

76. The use of claim 75, wherein the B cell malignancy is selected from multiple myeloma, leukemia and lymphoma.

77. The use of claim 76, wherein the B cell malignancy is multiple myeloma.

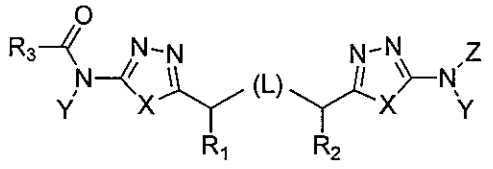
78. The use of claim 76, wherein the B cell malignancy is leukemia.

79. The use of claim 78, wherein the leukemia is selected from acute lymphoblastic leukemia and chronic lymphoblastic leukemia.

80. The use of claim 76, wherein the B cell malignancy is lymphoma.

81. The use of claim 80, wherein the lymphoma is selected from Burkitt's lymphoma, Diffuse large B cell lymphoma, follicular lymphoma and Hodgkin's lymphoma.

82. Use of a compound of formula I, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer,



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

wherein 1) the ratio of GLS to GS in cells of the cancer is determined; and 2) the medicament is administered if the ratio of GSL to GS is greater than or equal to 0.05.

83. The use of claim 82, wherein the compound is a compound as described in any of claims 2-23.

84. The use of claim any one of claims 82, wherein the ratio is greater than or equal to 1.

85. The use of any one of claims 82 or 84, wherein the ratio is determined by measuring the levels of GLS and GS in the cancer cells.

86. The use of claim 85, wherein measuring the levels of GLS and GS comprises measuring mRNA amounts.

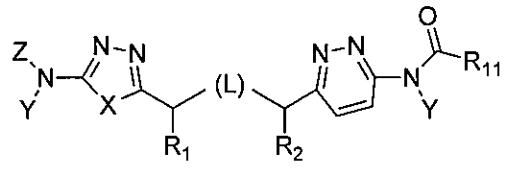
87. The use of claims 86, wherein measuring the levels of GLS and GS comprises measuring protein amounts.

88. The use of any one of claims 82-87, wherein GLS is GAC.

89. The use of any one of claims 82-87, wherein GLS is KGA.

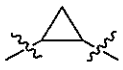
90. The use of any one of claims 82-87, wherein GLS is both GAC and KGA.

91. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer,



(Ia),

or a pharmaceutically acceptable salt thereof, wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl;

wherein 1) the ratio of GLS to GS in cells of the cancer is determined; and 2) the medicament is administered if the ratio of GLS to GS is greater than or equal to 0.05.

92. The use of claim 91, wherein the compound is a compound as described in any of claims 25-48.

93. The use of claim 91 or 92, wherein the ratio is greater than or equal to 1.

94. The use of any one of claims 91-93, wherein the ratio is determined by measuring the levels of GLS and GS in the cancer cells.

95. The use of claim 94, wherein measuring the levels of GLS and GS comprises measuring mRNA amounts.

96. The use of claims 94, wherein measuring the levels of GLS and GS comprises measuring protein amounts.

97. The use of any one of claims 91-96, wherein GLS is GAC.

98. The use of any one of claims 91-96, wherein GLS is KGA.

99. The use of any one of claims 91-96, wherein GLS is both GAC and KGA.

100. The use of any of claims 91-99, wherein the cancer is selected from a B cell malignancy, breast cancer, colorectal cancer, endocrine cancer, lung cancer, melanoma, mesothelioma and renal cancer.

101. The use of claim 100, wherein the cancer is breast cancer.

102. The use of claim 101, wherein the breast cancer comprises basal-type breast cancer cells, triple-negative breast cancer cells or claudin-low breast cancer cells.

103. The use of claim 101, wherein the breast cancer comprises basal-type breast cancer cells.

104. The use of claim 101, wherein the breast cancer comprises triple-negative breast cancer cells.

105. The use of claim 101, wherein the breast cancer comprises claudin-low breast cancer cells.

106. The use of claim 100, wherein the cancer is colorectal cancer.

107. The use of claim 100, wherein the cancer is endocrine cancer.

108. The use of claim 107, wherein the endocrine cancer is selected from adrenal cortex adenoma, adrenal cortex carcicnoma, adrenal gland pheochromocytoma and parathyroid gland adenoma.

109. The use of claim 100, wherein the cancer is melanoma.

110. The use of claim 100, wherein the cancer is renal cancer.

111. The use of claim 100, wherein the cancer is a B cell malignancy.

112. The use of claim 111, wherein the B cell malignancy is selected from multiple myeloma, leukemia and lymphoma.

113. The use of claim 111, wherein the B cell malignancy is multiple myeloma.

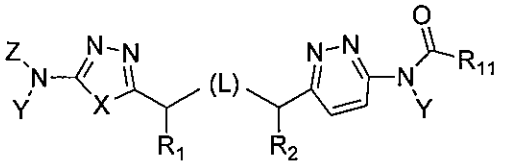
114. The use of claim 111, wherein the B cell malignancy is leukemia.

115. The use of claim 114, wherein the leukemia is selected from acute lymphoblastic leukemia and chronic lymphoblastic leukemia.

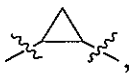
116. The use of claim 111, wherein the B cell malignancy is lymphoma.

117. The use of claim 116, wherein the lymphoma is selected from Burkitt's lymphoma, Diffuse large B cell lymphoma, follicular lymphoma and Hodgkin's lymphoma.

118. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer,


(Ia),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , preferably CH_2CH_2, wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X represents S, O or CH=CH, preferably S or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, arylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy, preferably H;

R_3 represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl,

cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

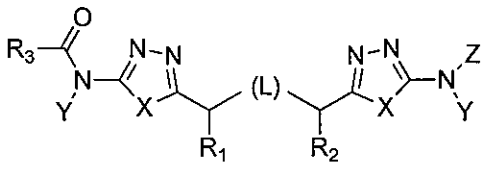
R_{11} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or $C(R_{12})(R_{13})(R_{14})$, $N(R_4)(R_{14})$ or OR_{14}, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_{12} and R_{13} each independently respresent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein both of R_{12} and R_{13} are not H; and

R_{14} represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl;

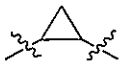
wherein 1) glutaminase activity in cells of the cancer is determined; and 2) the medicament is administered if the activity is greater than or equal to 0.005 μmol/min/mg of protein.

119. Use of a compound of formula Ia, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer,



(I),

wherein:

L represents CH_2SCH_2, CH_2CH_2, $CH_2CH_2CH_2$, CH_2, CH_2S, SCH_2, CH_2NHCH_2, CH=CH, or , wherein any hydrogen atom of a CH or CH_2 unit may be replaced by alkyl or alkoxy, any hydrogen of an NH unit may be replaced by alkyl, and any hydrogen atom of a CH_2 unit of CH_2CH_2, $CH_2CH_2CH_2$ or CH_2 may be replaced by hydroxy;

X, independently for each occurrence, represents S, O or CH=CH, wherein any hydrogen atom of a CH unit may be replaced by alkyl;

Y, independently for each occurrence, represents H or $CH_2O(CO)R_7$;

R_7, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclylalkyl, or heterocyclylalkoxy;

Z represents H or $R_3(CO)$;

R_1 and R_2 each independently represent H, alkyl, alkoxy or hydroxy;

R_3, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $C(R_8)(R_9)(R_{10})$, $N(R_4)(R_5)$ or OR_6, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_4 and R_5 each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$;

R_6, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy,

aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $C(O)R_7$; and

R_8, R_9 and R_{10} each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxycarbonyl, alkoxycarbonylamino, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R_8 and R_9 together with the carbon to which they are attached, form a carbocyclic or heterocyclic ring system, wherein any free hydroxyl group may be acylated to form $C(O)R_7$, and wherein at least two of R_8, R_9 and R_{10} are not H;

wherein 1) glutaminase activity in cells of the cancer is determined; and 2) the medicament is administered if the activity is greater than or equal to 0.005 μmol/min/mg of protein.