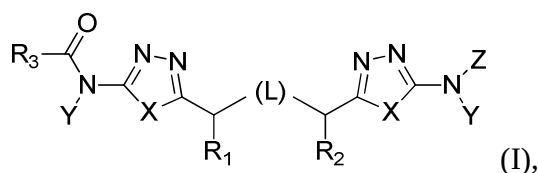


CLAIMS

1. Use of a glutaminase inhibitor in the manufacture of a medicament for treating or preventing cancer or a myeloproliferative disease, wherein the medicament is for conjoint administration with an anticancer agent selected from cabozantinib, axitinib, and an ALK inhibitor.
2. The use of claim 1, wherein the anticancer agent is selected from cabozantinib, crizotinib, and axitinib.
3. The use of claim 1 or claim 2, wherein the anticancer agent is cabozantinib.
4. The use of any one of claims 1-3, wherein the anticancer agent is crizotinib.
5. The use of any one of claims 1-3, wherein the anticancer agent is axitinib.
6. The use of any preceding claim, wherein the glutaminase inhibitor is a compound of formula I,



or a pharmaceutically acceptable salt thereof, wherein:

L represents CH₂SCH₂, CH₂CH₂, CH₂CH₂CH₂, CH₂, CH₂S, SCH₂, CH₂NHCH₂, CH=CH, or



, wherein any hydrogen atom of a CH or CH₂ 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 CH₂ unit of CH₂CH₂, CH₂CH₂CH₂ or CH₂ 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 CH₂O(CO)R₇;

R₇, independently for each occurrence, represents H or substituted or unsubstituted alkyl, alkoxy, aminoalkyl, alkylaminoalkyl, heterocyclalkyl, or heterocyclalkoxy;

Z represents H or R₃(CO);

R₁ and R₂ each independently represent H, alkyl, alkoxy or hydroxy;

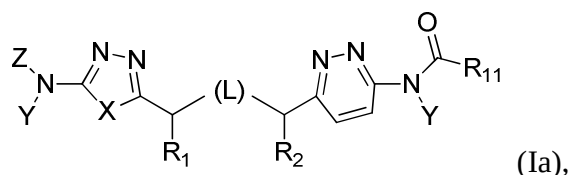
R₃, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or C(R₈)(R₉)(R₁₀), N(R₄)(R₅) or OR₆, wherein any free hydroxyl group may be acylated to form C(O)R₇;

R₄ and R₅ each independently represent H or substituted or unsubstituted alkyl, hydroxyalkyl, acyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form C(O)R₇;

R₆, independently for each occurrence, represents substituted or unsubstituted alkyl, hydroxyalkyl, aminoalkyl, acylaminoalkyl, alkenyl, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form C(O)R₇; and

R₈, R₉ and R₁₀ each independently represent H or substituted or unsubstituted alkyl, hydroxy, hydroxyalkyl, amino, acylamino, aminoalkyl, acylaminoalkyl, alkoxy, alkoxyalkyl, alkoxy, alkoxyalkyl, aryl, arylalkyl, aryloxy, aryloxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or R₈ and R₉ 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)R₇, and wherein at least two of R₈, R₉, and R₁₀ are not H.

7. The use of any one of claims 1-5, wherein the glutaminase inhibitor is a compound of formula Ia,



or a pharmaceutically acceptable salt thereof, wherein:

L represents CH_2SCH_2 , CH_2CH_2 , $\text{CH}_2\text{CH}_2\text{CH}_2$, CH_2 , CH_2S , SCH_2 , CH_2NHCH_2 , $\text{CH}=\text{CH}$, 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 , $\text{CH}_2\text{CH}_2\text{CH}_2$ or CH_2 may be replaced by hydroxy;

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

Y, independently for each occurrence, represents H or $\text{CH}_2\text{O}(\text{CO})\text{R}_7$;

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

Z represents H or $\text{R}_3(\text{CO})$;

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, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroaryloxyalkyl or $\text{C}(\text{R}_8)(\text{R}_9)(\text{R}_{10})$, $\text{N}(\text{R}_4)(\text{R}_5)$ or OR_6 , wherein any free hydroxyl group may be acylated to form $\text{C}(\text{O})\text{R}_7$;

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, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, wherein any free hydroxyl group may be acylated to form $\text{C}(\text{O})\text{R}_7$;

R₆, 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)R₇; and

R₈, R₉ and R₁₀ 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 R₈ and R₉ 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)R₇, and wherein at least two of R₈, R₉ and R₁₀ are not H;

R₁₁ represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl, or C(R₁₂)(R₁₃)(R₁₄), N(R₄)(R₁₄) or OR₁₄, wherein any free hydroxyl group may be acylated to form C(O)R₇;

R₁₂ and R₁₃ 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, wherein any free hydroxyl group may be acylated to form C(O)R₇, and wherein both of R₁₂ and R₁₃ are not H; and

R₁₄ represents substituted or unsubstituted aryl, arylalkyl, aryloxy, aryloxyalkyl, heteroaryl, heteroarylalkyl, heteroaryloxy, or heteroaryloxyalkyl.

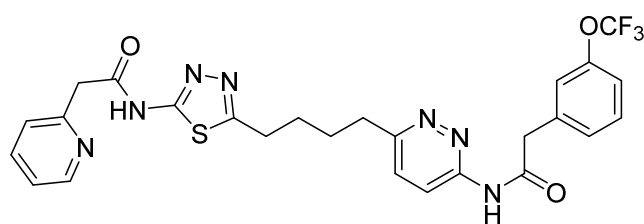
8. The use of claim 7, wherein R₁₁ represents substituted or unsubstituted arylalkyl.

9. The use of claim 7 or claim 8, wherein R₁₁ represents substituted or unsubstituted benzyl.

10. The use of any one of claims 7-9, wherein one or more of (a) – (e) applies:

- (a) L represents CH₂SCH₂, CH₂CH₂, CH₂S or SCH₂, preferably CH₂CH₂;
- (b) Y represents H;
- (c) X represents S or CH=CH, preferably S;
- (d) Z represents R₃(CO); or
- (e) R₁ and R₂ each represent H.

11. The use of any one of claims 7-10, wherein R₃ and R₁₁ are not identical.
12. The use of any one of claims 7-11, wherein R₃ represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl.
13. The use of any one of claims 7-12, wherein R₃ represents substituted or unsubstituted heteroarylalkyl.
14. The use of claim 7, wherein L represents CH₂SCH₂, CH₂CH₂, CH₂S, or SCH₂, Y represents H, X represents S, Z represents R₃(CO), R₁ and R₂ each represent H, R₃ represents substituted or unsubstituted arylalkyl, heteroarylalkyl, cycloalkyl or heterocycloalkyl, and R₁₁ represents substituted or unsubstituted arylalkyl; preferably wherein R₃ represents substituted or unsubstituted heteroarylalkyl.
15. The use of any preceding claim, wherein the glutaminase inhibitor is a compound having the structure of formula (II):



(II), or a pharmaceutically acceptable salt

thereof.

16. The use of any preceding claim, wherein the medicament is for treating or preventing cancer, wherein the cancer is selected from brain tumor, breast cancer, hepatocellular cancer,

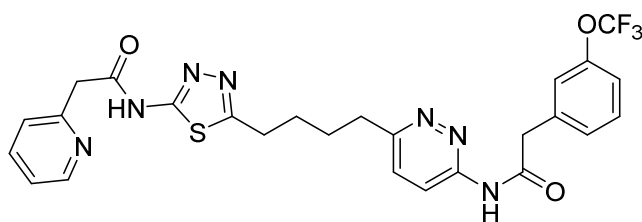
lung cancer including non-small cell lung cancer and small cell lung cancer, melanoma, ovarian cancer, prostate cancer, and renal cell cancer.

17. The use of claim 16, wherein the cancer is non-small cell lung cancer.

18. The use of claim 16, wherein the cancer is renal cell cancer.

19. The use of any one of claims 16-18, wherein the cancer is resistant to an anticancer agent selected from cabozantinib, crizotinib, and axitinib.

20. The use of claim 3, wherein the glutaminase inhibitor is a compound of formula II:

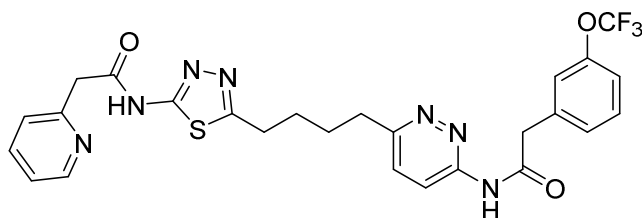


(II), or a pharmaceutically acceptable salt

thereof; and

the cancer is renal cell carcinoma, breast cancer, brain tumor, hepatocellular cancer, non-small cell lung cancer, melanoma, ovarian cancer, or prostate cancer, preferably renal cell carcinoma.

21. The use of claim 4, wherein the glutaminase inhibitor is a compound of formula II:

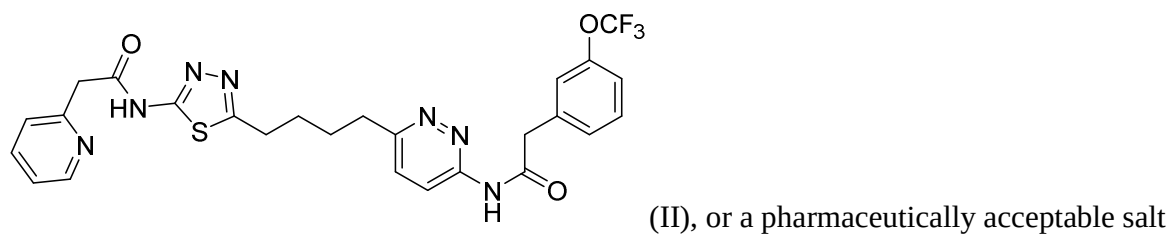


(II), or a pharmaceutically acceptable salt

thereof; and

the cancer is non-small cell lung cancer.

22. The use of claim 5, wherein the glutaminase inhibitor is a compound of formula II:



thereof; and

the cancer is renal cell carcinoma.

23. A pharmaceutical composition comprising a glutaminase inhibitor and an anticancer agent selected from cabozantinib, crizotinib, and axitinib.