Claims

1. A combination of a compound of formula (I), or a pharmaceutically acceptable salt thereof, and an anti-cancer agent selected from the group consisting of a taxane compound, a fluorine-containing nucleoside, a platinum compound, an analogue of camptothecin, a fluoropyrimidine compound and prodrugs thereof, or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer, wherein the compound of formula (I) is selected from the group consisting of:

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-thiazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-[(1R)-2-hydroxy-1-{4-[4-(hydroxymethyl)-1,3-thiazol-5-yl]phenyl}ethyl]-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(1-methyl-1H-pyrazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-N-{(1R)-1-[4-(1-ethyl-1H-pyrazol-5-yl)phenyl]-2-hydroxyethyl}-4-hydroxy-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-thiazol-5-

yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-N-{(1R)-1-[4-(1-ethyl-1H-pyrazol-5-yl)phenyl]-2-hydroxyethyl}-4-hydroxy-L-prolinamide, and

(4R)-1-[(2S)-2-(4-{4-[({6-Cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-oxazol-5-yl)phenyl]ethyl}-L-prolinamide.

2. Use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, according to Claim 1, in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered with an anti-cancer agent selected from the group consisting of a taxane compound, a fluorine-containing nucleoside, a platinum compound, an analogue of camptothecin, a fluoropyrimidine compound and prodrugs thereof, or a pharmaceutically acceptable salt thereof.

3. A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, according to Claim 1 and an anti-cancer agent selected from the group consisting of a taxane compound, a fluorine-containing nucleoside, a platinum compound, an analogue of camptothecin, a fluoropyrimidine compound and prodrugs thereof, or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutical acceptable excipient.

4. A pharmaceutical composition according to Claim 3 for use in the treatment of cancer.

5. Use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, according to Claim 1 and a therapeutically effective amount of an anti-cancer agent selected from the group consisting of a taxane compound, a fluorine-containing nucleoside, a platinum compound, an analogue of camptothecin, a fluoropyrimidine compound and prodrugs thereof, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

6. A kit-of-parts comprising:

(A) a pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, according to Claim 1, and optionally one or more pharmaceutically acceptable excipient, and

(B) a pharmaceutical composition comprising an anti-cancer agent selected from the group consisting of a taxane compound, a fluorine-containing nucleoside, a platinum compound, an analogue of camptothecin, a fluoropyrimidine compound and prodrugs thereof, or a pharmaceutically acceptable salt thereof, and optionally one or more pharmaceutically acceptable excipient,

which components (A) and (B) are each provided in a form that is suitable for administration in conjunction with the other,

for use in the treatment of cancer.

7. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use, or kit-of-parts for use according to any one of Claims 1 to 6, wherein the anti-cancer agent is a taxane compound.

8. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 7, wherein the taxane compound is paclitaxel.

9. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 7, wherein the taxane compound is docetaxel.

10. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 6, wherein the anti-cancer agent is a fluorine-containing nucleoside.

11. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 10, wherein the fluorine-containing nucleoside is gemcitabine.

12. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 6, wherein the anti-cancer agent is a platinum compound.

13. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 12, wherein the platinum compound is oxaliplatin.

14. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 6, wherein the anti-cancer agent is an analogue of camptothecin.

15. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 14, wherein the analogue of camptothecin is irinotecan.

16. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 6, wherein the anti-cancer agent is a fluoropyrimidine compound.

17. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 16, wherein the fluoropyrimidine compound is 5-FU.

18. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 17 wherein the cancer is pancreatic cancer.

19. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 17, wherein the cancer is colorectal cancer.

20. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 17, wherein the cancer is lung cancer.

21. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 20, wherein the compound of formula (I) is selected from the group consisting of:

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-

methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-thiazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-[(1R)-2-hydroxy-1-{4-[4-(hydroxymethyl)-1,3-thiazol-5-yl]phenyl}ethyl]-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(1-methyl-1H-pyrazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-N-{(1R)-1-[4-(1-ethyl-1H-pyrazol-5-yl)phenyl]-2-hydroxyethyl}-4-hydroxy-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-thiazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-N-{(1R)-1-[4-(1-ethyl-1H-pyrazol-5-yl)phenyl]-2-hydroxyethyl}-4-hydroxy-L-prolinamide, and

(4R)-1-[(2S)-2-(4-{4-[({(7M)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-oxazol-5-yl)phenyl]ethyl}-L-prolinamide.

22. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to any one of Claims 1 to 20, wherein the compound of formula (I) is selected from the group consisting of:

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-thiazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-[(1R)-2-hydroxy-1-{4-[4-(hydroxymethyl)-1,3-thiazol-5-yl]phenyl}ethyl]-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(1-methyl-1H-pyrazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(oxan-4-yl)oxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-N-{(1R)-1-[4-(1-ethyl-1H-pyrazol-5-yl)phenyl]-2-hydroxyethyl}-4-hydroxy-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-thiazol-5-yl)phenyl]ethyl}-L-prolinamide,

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-N-{(1R)-1-[4-(1-ethyl-1H-pyrazol-5-yl)phenyl]-2-hydroxyethyl}-4-hydroxy-L-prolinamide, and

(4R)-1-[(2S)-2-(4-{4-[({(7P)-6-cyclopropyl-4-[(1S,4S)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-7-(6-fluoro-5-methyl-1H-indazol-4-yl)-2-[(2S)-2-methoxypropoxy]quinazolin-8-yl}oxy)methyl]phenyl}-1H-1,2,3-triazol-1-yl)-3-methylbutanoyl]-4-hydroxy-N-{(1R)-2-hydroxy-1-[4-(4-methyl-1,3-oxazol-5-yl)phenyl]ethyl}-L-prolinamide.