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 CDK4/6 inhibitor, an SHP2 inhibitor, an EGFR inhibitor, a mTOR inhibitor, an immune checkpoint inhibitor, a PI3K inhibitor, an SOS1 inhibitor, and an AURK inhibitor, 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 CDK4/6 inhibitor, an SHP2 inhibitor, an EGFR inhibitor, a mTOR inhibitor, an immune checkpoint inhibitor, a PI3K inhibitor, an SOS1 inhibitor, and an AURK inhibitor, 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 CDK4/6 inhibitor, an SHP2 inhibitor, an EGFR inhibitor, a mTOR inhibitor, an immune checkpoint inhibitor, a PI3K inhibitor, an SOS1 inhibitor, and an AURK inhibitor, 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 an anti-cancer agent selected from the group consisting of a CDK4/6 inhibitor, an SHP2 inhibitor, an EGFR inhibitor, a mTOR inhibitor, an immune checkpoint inhibitor, a PI3K inhibitor, an SOS1 inhibitor, and an AURK inhibitor, 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 CDK4/6 inhibitor, an SHP2 inhibitor, an EGFR inhibitor, a mTOR inhibitor, an immune checkpoint inhibitor, a PI3K inhibitor, an SOS1 inhibitor, and an AURK inhibitor, 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 CDK4/6 inhibitor.

8. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 7, wherein the CDK4/6 inhibitor is Palbociclib.

9. 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 SHP2 inhibitor.

10. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 9, wherein the SHP2 inhibitor is TNO155.

11. 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 EGFR inhibitor.

12. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 11, wherein the EGFR inhibitor is Afatinib.

13. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 11, wherein the EGFR inhibitor is Cetuximab.

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 mTOR inhibitor.

15. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 14, wherein the mTOR inhibitor is Everolimus.

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 an immune checkpoint inhibitor.

17. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 16, wherein the immune checkpoint inhibitor is an anti-PD-1 antibody.

18. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 17, wherein the anti-PD-1 antibody is Nivolumab.

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 6, wherein the anti-cancer agent is a PI3K inhibitor.

20. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 19, wherein the PI3K inhibitor is Alpelisib.

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 6, wherein the anti-cancer agent is an SOS1 inhibitor.

22. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 21, wherein the SOS1 inhibitor is MRTX0902.

23. 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 AURK inhibitor.

24. The combination for use, pharmaceutical composition, pharmaceutical composition for use, use or kit-of-parts for use according to Claim 23, wherein the AURK inhibitor is Alisertib.

25. 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 24, wherein the cancer is pancreatic cancer.

26. 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 24, wherein the cancer is colorectal cancer.

27. 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 24, wherein the cancer is lung cancer.

28. 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 27, 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.

29. 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 27, 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.