CLAIMS

1. Use of a combination of a TEAD inhibitor and a KRAS G12C inhibitor in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein the TEAD inhibitor is selected from:

a) 4-((2S,4S)-5-Chloro-6-fluoro-2-phenyl-2-((S)-pyrrolidin-2-yl)-2,3-dihydrobenzofuran-4-yl)-5-fluoro-6-(2-hydroxyethoxy)-N-methylnicotinamide), or a pharmaceutically acceptable salt thereof of, or

b) (2-((2S,3S,4S)-5-Chloro-6-fluoro-3-methyl-2-((methylamino)methyl)-2-phenyl-2,3-dihydrobenzofuran-4-yl)-3-fluoro-4-methoxybenzamide), or a pharmaceutically acceptable salt thereof

and wherein a therapeutically effective amount of the combination is to be administered to the subject.

2. A TEAD inhibitor for use in the treatment of cancer, wherein the treatment further comprises KRAS G12C inhibitor to be administered, wherein the TEAD inhibitor is selected from:

a) 4-((2S,4S)-5-Chloro-6-fluoro-2-phenyl-2-((S)-pyrrolidin-2-yl)-2,3-dihydrobenzofuran-4-yl)-5-fluoro-6-(2-hydroxyethoxy)-N-methylnicotinamide) or a pharmaceutically acceptable salt thereof of, or

b) (2-((2S,3S,4S)-5-Chloro-6-fluoro-3-methyl-2-((methylamino)methyl)-2-phenyl-2,3-dihydrobenzofuran-4-yl)-3-fluoro-4-methoxybenzamide) or a pharmaceutically acceptable salt thereof.

3. A combination comprising:

i) a TEAD inhibitor selected from:

a) 4-((2S,4S)-5-Chloro-6-fluoro-2-phenyl-2-((S)-pyrrolidin-2-yl)-2,3-dihydrobenzofuran-4-yl)-5-fluoro-6-(2-hydroxyethoxy)-N-methylnicotinamide) or a pharmaceutically acceptable salt thereof of, or

b) (2-((2S,3S,4S)-5-Chloro-6-fluoro-3-methyl-2-((methylamino)methyl)-2-phenyl-2,3-dihydrobenzofuran-4-yl)-3-fluoro-4-methoxybenzamide) or a pharmaceutically acceptable salt thereof, and

ii) a KRAS G12C inhibitor.

4. A KRAS G12C inhibitor for use in the treatment of cancer, wherein the treatment further a TEAD inhibitor to be administered, wherein the TEAD inhibitor is selected from:

a) 4-((2S,4S)-5-Chloro-6-fluoro-2-phenyl-2-((S)-pyrrolidin-2-yl)-2,3-dihydrobenzofuran-4-yl)-5-fluoro-6-(2-hydroxyethoxy)-N-methylnicotinamide) or a pharmaceutically acceptable salt thereof of, or

b) (2-((2S,3S,4S)-5-Chloro-6-fluoro-3-methyl-2-((methylamino)methyl)-2-phenyl-2,3-dihydrobenzofuran-4-yl)-3-fluoro-4-methoxybenzamide) or a pharmaceutically acceptable salt thereof.

5. The use according to claim 1, further comprises a SHP2 inhibitor to be administered.

6. The combination according to claim 3, where the combination further comprises a SHP2 inhibitor.

7. A SHP2 inhibitor for use in the treatment of cancer, wherein the treatment further comprises a TEAD inhibitor and a KRAS G12C inhibitor to be administered, wherein the TEAD inhibitor is selected from selected from:

a) 4-((2S,4S)-5-Chloro-6-fluoro-2-phenyl-2-((S)-pyrrolidin-2-yl)-2,3-dihydrobenzofuran-4-yl)-5-fluoro-6-(2-hydroxyethoxy)-N-methylnicotinamide) or a pharmaceutically acceptable salt thereof of, or

b) (2-((2S,3S,4S)-5-Chloro-6-fluoro-3-methyl-2-((methylamino)methyl)-2-phenyl-2,3-dihydrobenzofuran-4-yl)-3-fluoro-4-methoxybenzamide) or a pharmaceutically acceptable salt thereof.

8. The use according to claim 1 or claim 5, or the combination according to claim 3 or claim 6, wherein the KRAS G12C inhibitor is selected from 1-{6-[(4M)-4-(5-Chloro-6-methyl-1H-indazol-4-yl)-5-methyl-3-(1-methyl-1H-indazol-5-yl)-1H-pyrazol-1-yl]-2-azaspiro[3.3]heptan-2-yl}prop-2-en-1-one), sotorasib (Amgen), adagrasib (Mirati), D-1553 (InventisBio), BI1701963 (Boehringer), GDC6036 (Roche), JNJ74699157 (J&J), X-Chem KRAS (X-Chem), LY3537982 (Lilly), BI1823911 (Boehringer), AS KRAS G12C (Ascentage Pharma), SF KRAS G12C (Sanofi), RMC032 (Revolution Medicine), JAB-21822 (Jacobio Pharmaceuticals), AST-KRAS G12C (Allist Pharmaceuticals), AZ KRAS G12C (Astra Zeneca), NYU-12VC1 (New York University), and RMC6291 (Revolution Medicines), or a pharmaceutically acceptable salt thereof.

9. The use or the combination according to claim 8, wherein the KRAS G12C inhibitor is (1-{6-[(4M)-4-(5-Chloro-6-methyl-1H-indazol-4-yl)-5-methyl-3-(1-methyl-1H-indazol-5-yl)-1H-pyrazol-1-yl]-2-azaspiro[3.3]heptan-2-yl}prop-2-en-1-one) or AMG510, or a pharmaceutically acceptable salt thereof.

10. The use or the combination according to claim 9, wherein the KRAS G12C inhibitor is 1-{6-[(4M)-4-(5-Chloro-6-methyl-1H-indazol-4-yl)-5-methyl-3-(1-methyl-1H-indazol-5-yl)-1H-pyrazol-1-yl]-2-azaspiro[3.3]heptan-2-yl}prop-2-en-1-one), or a pharmaceutically acceptable salt thereof.

11. The use according to claim 5, or the combination according to claim 6, wherein the SHP2 inhibitor is selected from the group consisting of TNO155 (Novartis), JAB3068 (Jacobio), JAB3312 (Jacobio), RLY1971 (Roche), SAR442720 (Sanofi), RMC4550 (Revolution Medicines), RMC4630 (Revolution Medicines), BBP398 (Navire), BR790 (Shanghai Blueray), SH3809 (Nanjing Sanhome), PF0724982 (Pfizer), ERAS601 (Erasca), RX-SHP2 (Redx Pharma), ICP189 (InnoCare), HBI2376 (HUYA Bioscience), ETS001 (Shanghai ETERN Biopharma),

TAS-ASTX (Taiho & Otsuka Pharmas) and X-37-SHP2 (X-37), or a pharmaceutically acceptable salt thereof.

12. The use or the combination according to claim 11, wherein the SHP2 inhibitor is TNO155, or a pharmaceutically acceptable salt thereof.

13. The use according to any one of claims 1, 5 and 8-12, wherein the cancer is a TEAD dependent cancer.

14. The use according to any one of claims 1, 5 and 8-13, wherein the cancer is selected from the group consisting of breast cancer, lung cancer, ovarian cancer, kidney cancer, uterine cancer, colorectal cancer, malignant pleural mesothelioma, pancreatic cancer, prostate cancer, gastric cancer, gastrointestinal stromal tumor, esophageal cancer, liver cancer, medullobastoma, head and neck cancer, sarcoma, squamous cell carcinoma, epithelioid hemangioendothelioma, ependymal tumor and bone cancer.

15. The use according to any one of claims 1, 5 and 8-14, , wherein the TEAD inhibitor is to be administered on each of the first 3 days of a 7 day treatment cycle, and wherein the treatment is composed of at least two treatment cycles.

16. The combination according to claim 3 or claim 6, for use in the treatment of cancer.