SUMMARY

The present disclosure provides, in part, methods of treating abnormal cell growth (e.g., cancer) in a subject in need thereof. The methods comprise treating a subject in need thereof by administering a dual RAF/MEK inhibitor (e.g., VS-6766) or a pharmaceutically acceptable salt thereof in combination with an additional agent described herein (e.g., an anti-PD-1 antibody or an anti-PD-L1 antibody). The methods may further comprise administering to the subject a FAK inhibitor (e.g., defactinib) or a pharmaceutically acceptable salt thereof.

In one aspect, the present disclosure provides a use of a dual RAF/MEK inhibitor and an anti-PD-1 antibody in the manufacture of a medicament for combination therapy to treat cancer in a subject in need thereof. In another aspect, the present disclosure provides a use of a dual RAF/MEK inhibitor in the manufacture of a first medicament and use of an anti-PD-1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat cancer in a subject in need thereof. In yet another aspect, the present disclosure provides a use of a dual RAF/MEK inhibitor in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject in need thereof, wherein said medicament is to be administered in combination with an anti-PD-1 antibody.

In a further aspect, the present disclosure provides a use of a dual RAF/MEK inhibitor and an anti-PD-L1 antibody in the manufacture of a medicament for combination therapy to treat cancer in a subject in need thereof. In another aspect, the present disclosure provides a use of a dual RAF/MEK inhibitor in the manufacture of a first medicament and use of an anti-PD-L1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat cancer in a subject in need thereof. In yet another aspect, the present disclosure provides a use of a dual RAF/MEK inhibitor in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject in need thereof, wherein said medicament is to be administered in combination with an anti-PD-L1 antibody.

Thus, in an ~~aspect~~example, provided herein is a method of treating a cancer in a subject in need thereof, the method comprising administering to the subject a dual RAF/MEK inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-1 antibody, thereby treating the subject.

In another ~~aspect~~example, provided herein is a method of treating a cancer in a subject in need thereof, the method comprising administering to the subject a dual RAF/MEK

inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-L1 antibody, thereby treating the subject.

In another ~~aspect~~example, provided herein is a method of treating a cancer in a subject in need thereof, the method comprising administering to the subject a dual RAF/MEK inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-1 antibody and a FAK inhibitor, thereby treating the subject.

In another ~~aspect~~example, provided herein is a method of treating a cancer in a subject in need thereof, the method comprising administering to the subject a dual RAF/MEK inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-L1 antibody and a FAK inhibitor, thereby treating the subject.

In some ~~embodiment~~examples, the dual RAF/MEK inhibitor is VS-6766 or a pharmaceutically acceptable salt thereof.

In some ~~embodiment~~examples, the dual RAF/MEK inhibitor is dosed at least once a week. In some ~~embodiment~~examples, the dual RAF/MEK inhibitor is dosed twice a week. In some ~~embodiment~~examples, the dual RAF/MEK inhibitor is dosed twice a week cyclically for three weeks on and then one week off. In some ~~embodiment~~examples, the cycle is repeated at least once.

In some ~~embodiment~~examples, the dual RAF/MEK inhibitor is dosed at about 0.8 mg to about 10 mg per administration. In some ~~embodiment~~examples, the dual RAF/MEK inhibitor is dosed at about 3.2 mg per administration. In some ~~embodiment~~examples, the dual RAF/MEK inhibitor is dosed at about 4 mg per administration.

In some ~~embodiment~~examples, the anti-PD-1 antibody is selected from the group consisting of balstilimab, camrelizumab, cemiplimab, dostarlimab, geptanolimab, nivolumab, pembrolizumab, penpulimab, pidilizumab, prolgolimab, retifanlimab, sasanlimab, serplulimab, serplulimab, sintilimab, spartalizumab, sulituzumab, tebotelimab, teripalimab, tislelizumab, toripalimab, toripalimab, zimberelimab, AMP-224 (MedImunne), AMP-514 (MedImunne), AT-16201 (AIMM Therapeutics BV), AVI-102 (AbVision Inc), BAT-1308 (Bio-Thera Solutions Ltd), BH-2950 (Beijing Hanmi Pharmaceutical Co Ltd), BSI-050K01 (Biosion Inc), CB-201 (Crescendo Biologics Ltd), CYTO-101 (Cytocom Inc), DB-004 (DotBio Pte Ltd), EX-105 (Excelmab Inc), EX-108 (Excelmab Inc), GNR-051 (Generium), HAB-21 (Suzhou Stainwei Biotech Inc), IBI-319 (Innovent Biologics Inc), IBI-321 (Innovent Biologics Inc), IKT-202 (Icell Kealex Therapeutics LLC), IMU-201 (Imugene Ltd), JS-201 (Shanghai Junshi Bioscience Co Ltd), LBL-006 (Leads Biolabs Inc), LBL-024 (Leads Biolabs Inc), LD-01 (Leidos Health Holdings LLC), LQ-005 (Shanghai Novamab Biopharmaceuticals Co Ltd), LQ-008 (Shanghai Novamab Biopharmaceuticals Co Ltd), MD-402 (MD Biosciences GmbH), OT-2 (OncoTrap Inc), PE-0105 (Shanghai Yunyi Health Technology Development Co Ltd), PF-07209960 (Pfizer Inc), PH-762 (Phio Pharmaceuticals Corp), REGN-PD-1/XX (Regeneron), RO7121661 (Genentech), SAUG-1 (Juvenescence UK Ltd), SCT-I10A (Sinocelltech), SG-001 (CSPC Pharmaceutical Group Ltd), SI-B003 (SystImmune), SL-279137 (Shattuck Labs), SSI-361 (Lyvgen Biopharma Ltd), STI-A1110 (Servier), STM-418 (Stcube Inc), Sym-021 (Symphogen A/S), TSR-075 (GlaxoSmithKline Plc), TY101 (Tayu Huaxia Biotech), Twist-PD-1 (Twist Bioscience), XmAb-TGFβR2 (Xencor), XmAb-YYCD28 (Xencor), XmAb20717 (Xencor), XmAb23104 (Xencor), YBL-006 (Y Biologics), YBL-019 (Y Biologics), and mDX-400 (Merck & Co Inc). In some ~~embodiment~~examples, the anti-PD-1 antibody is selected from the group consisting of cemiplimab, nivolumab, pembrolizumab, pidilizumab, spartalizumab, camrelizumab, sintilimab, tislelizumab, toripalimab, dostarlimab, AMP-224, and AMP-514.

In some ~~embodiment~~examples, the anti-PD-L1 antibody is selected from the group consisting of atezolizumab, avelumab, durvalumab, envafolimab, socazolimab, sugemalimab, ABM-101 (Abeome Corp), AP-505 (AP Biosciences Inc), APL-801 (Apollomics Inc), ATG-101 (Antengene Corp Ltd), AVA-027 (Avacta Life Sciences Ltd), AUNP12 (Aurigene), B-1961 (AP Biosciences Inc), BH-3120 (Hanmi Pharmaceuticals Co Ltd), BMS-986189 (Bristol Myers Squibb), BPI-9220 (Beta Pharma Inc), BPI-9320 (Beta Pharma Inc), CA-170 (Curis Inc), CCX-559 (ChemoCentryx Inc), CK-301 (cosibelimab), CS-17938 (Shenzhen Chipscreen Biosciences Co Ltd), CTX-8371 (Compass Therapeutics Inc), CYTCDR-2

(CytImmune Sciences Inc), DB-003 (DotBio Pte Ltd), DF-002 (Suzhou Dingfu Target Biotechnology Co Ltd), DPDL-1E (Shanghai Hycharm Inc), DR-30207 (Zhejiang Doer Biologics Corp), DSP-105 (KAHR medical Ltd), DSP-502 (KAHR medical Ltd), EI-011 (Elixiron Immunotherapeutics Inc), EI-014 (Elixiron Immunotherapeutics Inc), EMB-08 (EpimAb Biotherapeutics Inc), ENN-101 (Ennovabio), ENN-102 (Ennovabio), GB-7003 (Shanghai GeneChem Co Ltd), Gensci-047 (GeneScience Pharmaceuticals Co Ltd), HB-0025 (Huabo Biopharm (Shanghai) Co Ltd), HB-0028 (Huabo Biopharm (Shanghai) Co Ltd), HB-0036 (Huabo Biopharm (Shanghai) Co Ltd), HBM-7015 (Harbour BioMed (Guangzhou) Co Ltd), IBI-327 (Innovent Biologics Inc), IGM-7354 (IGM Biosciences Inc), IKT-201 (Icell Kealex Therapeutics LLC), IMC-2101 (ImmuneOncia Therapeutics LLC), IMC-2102 (ImmuneOncia Therapeutics LLC), IMGS-002 (Immunogenesis Inc), IMM-2510 (ImmuneOnco Biopharmaceuticals (Shanghai) Co Ltd), INBRX-105 (Elpiscience Biopharmaceutical Ltd), JBI-426 (Jubilant Therapeutics Inc), JNB-809 (JN Biosciences LLC), JNB-813 (JN Biosciences LLC), KN-052 (Alphamab Oncology), KY-1043 (Kymab Ltd), LP-008 (Lepu Biopharma Co Ltd), LQ-002 (Shanghai Novamab Biopharmaceuticals Co Ltd), LQ-004 (Shanghai Novamab Biopharmaceuticals Co Ltd), LVGN-1673 (Lyvgen Biopharma Ltd), LY-3434172 (Eli Lilly and Co), LYN-102 (LynkCell Inc), MCLA-145 (Merus NV), MEDI-7526 (AstraZeneca Plc), PH-790 (Phio Pharmaceuticals Corp), PM-1003 (Biotheus Inc), PRS-344 (Pieris Pharmaceuticals Inc), Q-1802 (QureBio), QL-301 (QLSF Biotherapeutics Inc), QLS31901 (Qilu Pharmaceutical), RC98 (RemeGen), SHR-1316 (Jiangsu Hengrui Medicine Co Ltd), SHR-1701 (Jiangsu Hengrui Medicine Co Ltd), SIM-236 (Jiangsu Simcere Pharmaceutical Co Ltd), SL-279252 (Shattuck Labs Inc), SL-279258 (Shattuck Labs Inc), SLSP-03 (Salspera LLC), SNA-02 (Oneness Biotech Co Ltd), STT-01 (Stcube Inc), TI-1007 (Timmune Biotech), TJ-L1C4 (I-Mab Biopharma), TJ-L1D5 (I-Mab Biopharma), TJ-L1H3 (I-Mab Biopharma), TJ-L1I7 (I-Mab Biopharma), TJL-14B (I-Mab Biopharma), TS1905 (Luye Pharma Group), TST-005 (Transcenta Holding Ltd), TTXsiPDL-1 (Transcode Therapeutics Inc), TXB-4BC3 (Ossianix Inc), VXM-10 (Vaximm AG), YBL-007 (Y-Biologics Inc), YBL-008 (Y-Biologics Inc), YBL-009 (Y-Biologics Inc), YBL-013 (Y-Biologics Inc), YBL-016 (Y-Biologics Inc), YBL-020 (Y-Biologics Inc). In some ~~embodiment~~examples, the anti-PD-L1 antibody is selected from the group consisting of avelumab, durvalumab, atezolizumab, KN035, CK-301, AUNP12, CA-170, and BMS-986189.

In some ~~embodiment~~examples, the FAK inhibitor is defactinib.

In some ~~embodiment~~examples, the cancer is a cancer characterized as having a RAS mutation. In some ~~embodiment~~examples, the cancer is a cancer characterized as having a RAF mutation. In

some ~~embodiment~~examples, the cancer is a cancer characterized as having a KRAS, NRAS, HRAS, and/or BRAF mutation.

In some ~~embodiment~~examples, the cancer is lung adenocarcinoma, colorectal cancer, uveal melanoma, ovarian cancer, uterine endometrioid carcinoma, bladder urothelial carcinoma, breast invasive lobular carcinoma, cervical squamous cell carcinoma, cutaneous melanoma, endocervical adenocarcinoma, hepatocellular carcinoma, pancreatic adenocarcinoma, biphasic type pleural mesothelioma, renal clear cell carcinoma, renal clear cell carcinoma, stomach adenocarcinoma, tubular stomach adenocarcinoma, uterine carcinosarcoma, or uterine malignant mixed Mullerian tumor.

Other objects and advantages will become apparent to those skilled in the art from a consideration of the ensuing Detailed Description, Examples, and Claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows that VS-6766 upregulates markers associated with antigen presentation.

FIG. 2A shows exemplary tumor volume changes in CT26 xenografts after treatment with VS-6766 and/or anti-PD-1 antibody.

FIG. 2B shows exemplary tumor volume changes in CT26 mice treated with VS-6766 and/or anti-PD-1 antibody.

FIG. 2C shows an exemplary Kaplan-Meier survival curve of CT26 mice treated with VS-6766 and/or anti-PD-1 antibody.

FIG. 3A shows immune memory in an exemplary CT26 colorectal cancer model.

FIG. 3B shows exemplary effector memory in CD4 or CD8 cells.

FIG. 4A shows exemplary antitumor effects of VS-6766 + anti-PD-1 in combination with a FAK inhibitor.

FIG. 4B shows exemplary antitumor effects of VS-6766 + FAK inhibitor in combination with an anti-PD-1.

DETAILED DESCRIPTION

As generally described herein, the present disclosure provides methods and combinations of compounds useful for treating abnormal cell growth (e.g., cancer) in a subject in need thereof.

CLAIMS

1. Use of a~~A~~ dual RAF/MEK inhibitor and an anti-PD-1 antibody in the manufacture of a medicament for combination therapy to ~~method of~~ treat~~ing a~~ cancer in a subject in need thereof~~, the method comprising administering to the subject a dual RAF/MEK inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-1 antibody, thereby treating the subject~~.

2. Use of a dual RAF/MEK inhibitor in the manufacture of a first medicament and use of an anti-PD-1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat cancer in a subject in need thereof.

3. Use of a dual RAF/MEK inhibitor in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject in need thereof, wherein said medicament is to be administered in combination with an anti-PD-1 antibody.

~~2~~4. The use ~~method~~ of any one of claims 1-3, wherein the dual RAF/MEK inhibitor is VS-6766 or a pharmaceutically acceptable salt thereof.

~~3~~5. The use ~~method~~ of any one of claims 1-~~4 or 2~~, wherein the dual RAF/MEK inhibitor is to be dosed a) at least once a week; b) ~~.~~

~~4. The method of any one of claims 1-3, wherein the dual RAF/MEK inhibitor is dosed~~ twice a week; ~~.~~

~~5. The method of claim 1 or 2, wherein the dual RAF/MEK inhibitor is dosed~~or c) twice a week ~~cyclically~~ as a cycle, wherein the cycle comprises that the dual RAF/MEK inhibitor is to be administered for three weeks and then the dual RAF/MEK inhibitor to be administered ~~on and then~~for one week ~~off~~, optionally ~~.~~

~~6. The method of claim 5,~~ wherein the cycle is repeated at least once.

~~7~~6. The use ~~method~~ of any one of claims 1-~~6~~5, wherein the dual RAF/MEK inhibitor is to be dosed at ~~about~~ 0.8 mg to ~~about~~ 10 mg per administration, ~~.~~

~~8. The method of any one of claims 1-7, wherein the dual RAF/MEK inhibitor is dosed at~~ about 3.2 mg per administration, or ~~.~~

~~9. The method of any one of claims 1-7, wherein the dual RAF/MEK inhibitor is dosed at~~ about 4 mg per administration.

~~10~~7. The use ~~method~~ of any one of claims 1-~~9~~6, wherein the anti-PD-1 antibody is selected from the group consisting of balstilimab, camrelizumab, cemiplimab, dostarlimab, geptanolimab, nivolumab, pembrolizumab, penpulimab, pidilizumab, prolgolimab, retifanlimab, sasanlimab, serplulimab, serplulimab, sintilimab, spartalizumab, sulituzumab, tebotelimab, teripalimab, tislelizumab, toripalimab, toripalimab, zimberelimab, AMP-224, AMP-514, AT-16201, AVI-102, BAT-1308, BH-2950, BSI-050K01, CB-201, CYTO-101, DB-004, EX-105, EX-108, GNR-051, HAB-21, IBI-319, IBI-321, IKT-202, IMU-201, JS-201, LBL-006, LBL-024, LD-01, LQ-005, LQ-008, MD-402, OT-2, PE-0105, PF-07209960, PH-762, REGN-PD-1/XX, RO7121661, SAUG-1, SCT-I10A, SG-001, SG001, SI-B003, SL-279137, SSI-361, STI-A1110, STM-418, Sym-021, TSR-075, TY101, Twist-PD-1, XmAb-TGFβR2, XmAb-YYCD28, XmAb20717, XmAb23104, YBL-006, YBL-019, and mDX-400.

~~11~~8. The use ~~method~~ of any one of claims 1-~~10~~7, wherein the anti-PD-1 antibody is to be dosed a) at least once a week; b) ~~.~~

~~12. The method of any one of claims 1-10, wherein the anti-PD-1 antibody is dosed~~ every two weeks; c) ~~.~~

~~13. The method of any one of claims 1-10, wherein the anti-PD-1 antibody is dosed~~ every three weeks; d) ~~.~~

~~14. The method of any one of claims 1-10, wherein the anti-PD-1 antibody is dosed~~ every four weeks; or ~~.~~e)

~~15. The method of any one of claims 1-10, wherein the anti-PD-1 antibody is dosed~~ every six weeks.

~~16~~9. The use ~~method~~ of any one of claims 1-~~15~~8, wherein the anti-PD-1 antibody is to be dosed at ~~about~~ 100 mg to ~~about~~ 1000 mg per administration.

~~17~~10. The use ~~method~~ of any one of claims 1-~~16~~9, wherein the anti-PD-1 antibody is to be administered parenterally.

~~18~~11. Use of a~~A~~ dual RAF/MEK inhibitor and an anti-PD-L1 antibody in the manufacture of a medicament for combination therapy to ~~method of~~ treat~~ing a~~ cancer in a subject in need thereof~~, the method comprising administering to the subject a dual RAF/MEK inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-L1 antibody, thereby treating the subject~~.

12. Use of a dual RAF/MEK inhibitor in the manufacture of a first medicament and use of an anti-PD-L1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat cancer in a subject in need thereof.

13. Use of a dual RAF/MEK inhibitor in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject in need thereof, wherein said medicament is to be administered in combination with an anti-PD-L1 antibody.

~~19~~14. The use ~~method~~ of any one of claims ~~18~~11-13, wherein the dual RAF/MEK inhibitor is VS-6766 or a pharmaceutically acceptable salt thereof.

~~20~~15. The use ~~method~~ ofany one of claims ~~18 or 19~~11-14, wherein the anti-PD-L1 antibody is selected from the group consisting of atezolizumab, avelumab, durvalumab, envafolimab, socazolimab, sugemalimab, ABM-101, AP-505, APL-801, ATG-101, AVA-027, AUNP12, B-1961, BH-3120, BMS-986189, BPI-9220, BPI-9320, CA-170, CCX-559, CK-301, CS-17938, CTX-8371, CYTCDR-2, DB-003, DPDL-1E, DR-30207, DSP-105, DSP-502, EI-011, EI-014, EMB-08, ENN-101, ENN-102, GB-7003, Gensci-047, HB-0025, HB-0028, HB-0036, HBM-7015, IBI-327, IGM-7354, IKT-201, IMC-2101, IMC-2102, IMGS-002, IMM-2510, INBRX-105, JBI-426, JNB-809, JNB-809, JNB-813, JNB-813, KN-052, KN035, KY-1043, LP-008, LQ-002, LQ-004, LVGN-1673, LY-3434172, LYN-102, MCLA-145, MEDI-7526, PH-790, PM-1003, PRS-344, Q-1802, QL-301, QLS31901, RC98, SHR-1316, SHR-1701, SIM-236, SL-279252, SL-279258, SLSP-03, SNA-02, STT-01, TI-1007, TJ-L1C4, TJ-L1D5, TJ-L1H3, TJ-L1I7, TJL-14B, TS1905, TST-005, TTXsiPDL-1, TXB-4BC3, VXM-10, YBL-007, YBL-008, YBL-009, YBL-013, YBL-016, and YBL-020.

~~21~~16. The use ~~method~~ of any one of claims ~~18-20~~11-15, wherein the anti-PD-L1 antibody is to be administered parenterally.

~~22~~17. The use ~~method~~ of any one of claims ~~18-21~~11-16, wherein the anti-PD-L1 antibody is to be administered a) every two weeks; b) ~~.~~

~~23. The method of any one of claims 18-21, wherein the anti-PD-L1 antibody is administered~~ every three weeks; or c) ~~.~~

~~24. The method of any one of claims 18-21, wherein the anti-PD-L1 antibody is administered~~ every four weeks.

~~25~~18. The use ~~method~~ of any one of claims ~~18-24~~11-17, wherein the anti-PD-L1 antibody is to be dosed at ~~about~~ 100 mg to ~~about~~ 2000 mg per administration.

~~26~~19. The use ~~method~~ of any one of claims ~~18-25~~11-18, wherein the dual RAF/MEK inhibitor is to be dosed at least once a week; b) ~~.~~

~~27. The method of any one of claims 18-26, wherein the dual RAF/MEK inhibitor is dosed~~ twice a week; c) ~~.~~

~~28. The method of any one of claims 18-25, wherein the dual RAF/MEK inhibitor is dosed~~ twice a week ~~cyclically~~ as a cycle, wherein the cycle comprises that the dual RAF/MEK inhibitor is to be administered for three weeks and then the dual RAF/MEK inhibitor is not to be administered for ~~on and then~~ one week ~~off~~, optionally ~~.~~

~~29. The method of claim 28,~~ wherein the cycle is repeated at least once.

~~30~~20. The use ~~method~~ of any one of claims ~~18-29~~11-19, wherein the dual RAF/MEK inhibitor is to be dosed at ~~about~~ 0.8 mg to ~~about~~ 10 mg per administration, ~~.~~

~~31. The method of any one of claims 18-30, wherein the dual RAF/MEK inhibitor is dosed at~~ about 3.2 mg per administration, or ~~.~~

~~32. The method of any one of claims 18-30, wherein the dual RAF/MEK inhibitor is dosed at~~ about 4 mg per administration.

~~33~~21. The use ~~method~~ of any one of claims 1-~~32~~20, ~~wherein the method~~ further ~~comprises~~ comprising that ~~administering to the subject~~ a FAK inhibitor or a pharmaceutically acceptable salt thereof is to be administered to the subject.

~~34~~22. The use ~~method~~ of claim ~~33~~21, wherein the FAK inhibitor is defactinib.

~~35~~23. The use ~~method~~ of claim ~~33~~21 or 22~~34~~, wherein the FAK inhibitor is to be dosed twice daily or ~~.~~

~~36. The method of claim 33 or 34, wherein the FAK inhibitor is dosed~~ once daily.

~~37~~24. The use ~~method~~ of any one of claims ~~33-36~~17-~~19~~21-23, wherein the FAK inhibitor is to be dosed at ~~about~~ 100 mg to ~~about~~ 1000 mg per administration, ~~.~~

~~38. The method of any one of claims 33-37, wherein the FAK inhibitor is dosed at about~~ 200 mg to ~~about~~ 400 mg per administration~~.~~,

~~39. The method of any one of claims 33-38, wherein the FAK inhibitor is dosed at~~ about 200 mg per administration, or ~~.~~

~~40. The method of any one of claims 33-38, wherein the FAK inhibitor is dosed at~~ about 400 mg per administration.

~~41~~25. The use ~~method~~ of any one of claims ~~33-40~~21-24, wherein the FAK inhibitor is to be administered orally.

~~42. A method of treating a cancer in a subject in need thereof, the method comprising administering to the subject a dual RAF/MEK inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-1 antibody and a FAK inhibitor, thereby treating the subject.~~

~~43. A method of treating a cancer in a subject in need thereof, the method comprising administering to the subject a dual RAF/MEK inhibitor or a pharmaceutically acceptable salt thereof in combination with an anti-PD-L1 antibody and a FAK inhibitor, thereby treating the subject.~~

~~44. The method of claim 42 or 43, wherein the dual RAF/MEK inhibitor is VS-6766 or a pharmaceutically acceptable salt thereof.~~

2645. The use ~~method~~ of any one of claims 1-~~44~~2125, wherein the cancer is a cancer characterized as having a RAS mutation, or ~~.~~

~~46. The method of any one of claims 1-45, wherein the cancer is a cancer characterized as having~~ a RAF mutation, or ~~.~~

~~47. The method of any one of claims 1-44, wherein the cancer is a cancer characterized as having~~ a KRAS, NRAS, HRAS, and/or BRAF mutation.

~~48~~27. The use ~~method~~ of any one of claims 1-~~47~~26, wherein the cancer is lung adenocarcinoma, colorectal cancer, uveal melanoma, ovarian cancer, uterine endometrioid carcinoma, bladder urothelial carcinoma, breast invasive lobular carcinoma, cervical squamous cell carcinoma, cutaneous melanoma, endocervical adenocarcinoma, hepatocellular carcinoma, pancreatic adenocarcinoma, biphasic type pleural mesothelioma, renal clear cell carcinoma, renal clear cell carcinoma, stomach adenocarcinoma, tubular stomach adenocarcinoma, uterine carcinosarcoma, or uterine malignant mixed Mullerian tumor.