

at a dose of 60 mg, on days 1-21 of a 28 day cycle; and (ii) Compound I, or a pharmaceutically acceptable salt thereof, at a dose of 960 mg twice daily, each day of the 28 day cycle.

[0015] ~~In one aspect, There are provided~~ are pharmaceutical products comprising (i) a first composition comprising [3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl][3-hydroxy-3-[(2S)-2-piperidinyl]-1-azetidiny]methanone (Compound II), or a pharmaceutically acceptable salt thereof; and (ii) a second composition comprising propane-1-sulfonic acid {3-[5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonyl]-2,4- difluoro-phenyl}-amide

(Compound I), or a pharmaceutically acceptable salt thereof; as a combined preparation for concurrent or sequential use in the treatment of BRAF^{V600} mutation-positive unresectable or metastatic melanoma, wherein the Compound II is administered at a dose of 60 mg, on days 1-21 of a 28 day cycle, and wherein Compound I is administered at a dose of 960 mg, twice daily each day of the 28 day cycle.

[0015a] In ~~another one~~ aspect, provided is use of a combination of (i) a first composition comprising [3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl][3-hydroxy-3-[(2S)-2-piperidinyl]-1-azetidiny]methanone (Compound II), or a pharmaceutically acceptable salt thereof; and (ii) a second composition comprising propane-1-sulfonic acid {3-[5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonyl]-2,4- difluoro-phenyl}-amide (Compound I), or a pharmaceutically acceptable salt thereof; in the manufacture of a medicament for the treatment of BRAF^{V600} mutation-positive unresectable or metastatic melanoma, wherein the Compound II is to be administered at a dose of 60 mg once daily, on days 1-21 of a 28 day cycle, concurrently or sequentially with Compound I that is to be administered at a dose of 960 mg, twice daily each day of the 28 day cycle.

[0016] In some embodiments, Compound I, or a pharmaceutically-acceptable salt thereof, is substantially in amorphous form. In some embodiments, Compound I, or a pharmaceutically-acceptable salt thereof, is in amorphous form. In some embodiments, Compound I, or a pharmaceutically-acceptable salt thereof, is contained in a solid molecular complex formed with hydroxypropyl methyl cellulose acetate succinate such that it is immobilized in its amorphous form. In some embodiments, the amounts of Compound I, or a pharmaceutically-acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of from about 1:9 to about 5:5, respectively. In some embodiments, the amounts of Compound I, or a pharmaceutically-acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of from about 2:8 to about 4:6, respectively. In some embodiments, the amounts of Compound I, or a pharmaceutically-acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of about 3:7, respectively. In some embodiments, the second composition comprises a blend wherein about 97% by weight of the blend is the aforementioned solid molecular complex and about 3% by weight of the blend is silicon dioxide. In some embodiments, the second composition comprises a

WHAT IS CLAIMED IS:

1. A pharmaceutical product comprising (i) a first composition comprising [3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl][3-hydroxy-3-[(2S)-2-piperidinyl]-1-azetidiny]methanone (Compound II); or a pharmaceutically acceptable salt thereof; and (ii) a second composition comprising propane-1-sulfonic acid {3-[5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonyl]-2,4-difluoro-phenyl}-amide (Compound I); or a pharmaceutically acceptable salt thereof; as a combined preparation for concurrent or sequential use in the treatment of BRAF^{V600}-mutation-positive unresectable or metastatic melanoma, wherein the Compound II is administered at a dose of 60 mg, on days 1-21 of a 28-day cycle, and wherein Compound I is administered at a dose of 960 mg, twice daily each day of the 28-day cycle.
2. The pharmaceutical product of claim 1, wherein the first composition is administered sequentially with the second composition.
3. The pharmaceutical product of claim 1, wherein the first composition is administered concurrently with the second composition.
4. The pharmaceutical product of claim 1, wherein the first and second compositions are co-formulated.
5. The pharmaceutical product of any one of claims 1-4, wherein Compound I, or a pharmaceutically acceptable salt thereof, is substantially in amorphous form.
6. The pharmaceutical product of any one of claims 1-4, wherein Compound I, or a pharmaceutically acceptable salt thereof, is in amorphous form.
7. The pharmaceutical product of any one of claims 1-6, wherein Compound I, or a pharmaceutically acceptable salt thereof, is contained in a solid molecular complex formed with hydroxypropyl methyl cellulose acetate succinate such that it is immobilized in its amorphous form.
8. The pharmaceutical product of claim 7, wherein the amounts of Compound I, or a pharmaceutically acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of from about 1:9 to about 5:5, respectively.
9. The pharmaceutical product of claim 7, wherein the amounts of Compound I, or a pharmaceutically acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of from about 2.8 to about 4.6, respectively.

~~10. The pharmaceutical product of claim 7, wherein the amounts of Compound I, or a pharmaceutically acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of about 3:7, respectively.~~

~~11. The pharmaceutical product of claim 7, wherein the amounts of Compound I, or a pharmaceutically acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of 3:7, respectively.~~

~~12. The pharmaceutical product of any one of claims 1-7, wherein the second composition comprises a blend wherein about 97% by weight of the blend is the solid molecular complex according to claim 7 and about 3% by weight of the blend is silicon dioxide.~~

~~13. The pharmaceutical product of any one of claims 1-7, wherein the second composition comprises a suspension of the solid molecular complex according to claim 7 in a pharmaceutically acceptable carrier.~~

~~14. The pharmaceutical product of any one of claims 1-7, wherein the second composition comprises a tablet comprising a solid molecular complex of Compound I, or a pharmaceutically acceptable salt thereof, and HPMC-AS.~~

~~15. The pharmaceutical product of any one of claims 1-14, wherein the first composition comprises one or more of lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, and magnesium stearate.~~

~~16. The pharmaceutical product of any one of claims 1-14, wherein Compound II is provided as a tablet comprising lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, and magnesium stearate.~~

~~17. The pharmaceutical product of claim 16, wherein the tablet comprises a tablet coating comprising polyvinyl alcohol part hydrolyzed, titanium dioxide, polyethylene glycol 3350, and talc.~~

~~18. The pharmaceutical product of any one of claims 1-17, wherein Compound II is provided as a 20 mg tablet, as a 40 mg tablet, or as a 60 mg tablet.~~

~~19. The pharmaceutical product of any one of claims 1-18, wherein a second 960 mg dose of Compound I, or a pharmaceutically acceptable salt thereof is administered about 12 hours after a first 960 mg dose of Compound I, or a pharmaceutically acceptable salt thereof.~~

~~20. The pharmaceutical product of any one of claims 1-19, wherein Compound I, or a pharmaceutically acceptable salt thereof, and Compound II, or a pharmaceutically acceptable salt thereof, are each administered orally, with or without food.~~

~~21. The pharmaceutical product of any one of claims 1-20, wherein the unresectable or metastatic melanoma is BRAF^{V600E}-mutation-positive melanoma.~~

~~22. The pharmaceutical product of any one of claims 1-21, wherein the unresectable or metastatic melanoma is metastatic melanoma.~~

~~23. The pharmaceutical product of any one of claims 1-22, wherein BRAF^{V600}-mutation is determined using a method comprising (a) performing PCR or sequencing on nucleic acid (e.g., DNA) extracted from a sample of the patient's melanoma; and (b) determining expression of BRAF^{V600} in the sample.~~

~~24. The pharmaceutical product of claim 23, wherein the melanoma sample is a formalin-fixed paraffin-embedded sample.~~

~~25. The pharmaceutical product of any of the preceding claims, wherein the patient's unresectable or metastatic melanoma has not been previously treated.~~

WHAT IS CLAIMED IS:

261. Use of a combination of (i) a first composition comprising [3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl][3-hydroxy-3-[(2S)-2-piperidinyl]-1-azetidiny]methanone (Compound II), or a pharmaceutically acceptable salt thereof; and (ii) a second composition comprising propane-1-sulfonic acid {3-[5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonyl]-2,4- difluoro-phenyl}-amide (Compound I), or a pharmaceutically acceptable salt thereof; in the manufacture of a medicament for the treatment of BRAF^{V600} mutation-positive unresectable or metastatic melanoma, wherein the Compound II is to be administered at a dose of 60 mg once daily, on days 1-21 of a 28 day cycle, concurrently or sequentially with Compound I that is to be administered at a dose of 960 mg, twice daily each day of the 28 day cycle.

272. The use of claim 261, wherein the first composition is to be administered sequentially with the second composition.

283. The use of claim 261, wherein the first composition is to be administered concurrently with the second composition.

~~29. The use of claim 26, wherein the first and second compositions are co-formulated.~~

304. The use of any one of claims 261-293, wherein Compound I, or a pharmaceutically-acceptable salt thereof, is substantially in amorphous form.

345. The use of any one of claims 261-293, wherein Compound I, or a pharmaceutically-acceptable salt thereof, is in amorphous form.

326. The use of any one of claims 261-345, wherein Compound I, or a pharmaceutically-acceptable salt thereof, is contained in a solid molecular complex formed with hydroxypropyl methyl cellulose acetate succinate such that it is immobilized in its amorphous form.

337. The use of claim 326, wherein the amounts of Compound I, or a pharmaceutically-acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of from about 1:9 to about 5:5, respectively.

348. The use of claim 326, wherein the amounts of Compound I, or a pharmaceutically-acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of from about 2.8 to about 4.6, respectively.

359. The use of claim 326, wherein the amounts of Compound I, or a pharmaceutically-acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of about 3:7, respectively.

3610. The use of claim 326, wherein the amounts of Compound I, or a pharmaceutically-acceptable salt thereof, and hydroxypropyl methyl cellulose acetate succinate in said complex are in a ratio of 3:7, respectively.

~~37~~11. The use of any one of claims ~~261-326~~, wherein the second composition comprises a blend wherein about 97% by weight of the blend is the solid molecular complex according to claim 32 and about 3% by weight of the blend is silicon dioxide.

~~38~~12. The use of any one of claims ~~261-326~~, wherein the second composition comprises a suspension of the solid molecular complex according to claim 32 in a pharmaceutically acceptable carrier.

~~39~~13. The use of any one of claims ~~261-326~~, wherein the second composition comprises a tablet comprising a solid molecular complex of Compound I, or a pharmaceutically- acceptable salt thereof, and HPMC-AS.

~~40~~14. The use of any one of claims ~~261-293~~, wherein the first composition comprises one or more of lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, and magnesium stearate.

~~41~~15. The use of any one of claims ~~261-293~~, wherein Compound II is provided as a tablet comprising lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, and magnesium stearate.

~~42~~16. The use of claim ~~41~~15, wherein the tablet comprises a tablet coating comprising polyvinyl alcohol-part hydrolyzed, titanium dioxide, polyethylene glycol 3350, and talc.

~~43~~17. The use of any one of claims ~~261-4216~~, wherein Compound II is provided as a 20 mg tablet, as a 40 mg tablet, or as a 60 mg tablet.

~~44~~18. The use of any one of claims ~~261-4317~~, wherein a second 960 mg dose of Compound I, or a pharmaceutically acceptable salt thereof is administered about 12 hours after a first 960 mg dose of Compound I, or a pharmaceutically acceptable salt thereof.

~~45~~19. The use of any one of claims ~~261-4418~~, wherein Compound I, or a pharmaceutically acceptable salt thereof, and Compound II, or a pharmaceutically acceptable salt thereof, are each administered orally, with or without food.

~~46~~20. The use of any one of claims ~~261-4519~~, wherein the patient's unresectable or metastatic melanoma has not been previously treated.