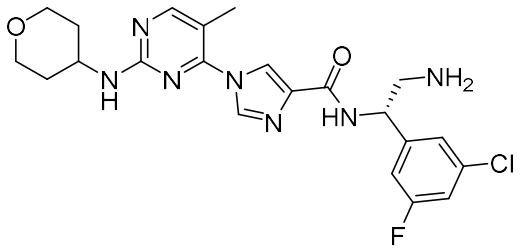
CLAIMS

1. Use of:

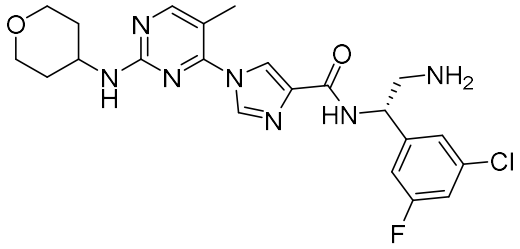


(i) compound 1: , or a pharmaceutically acceptable salt thereof; and

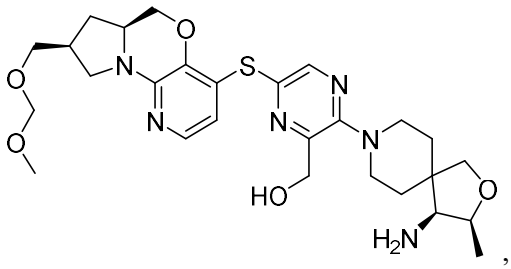
(ii) a SHP2 inhibitor,

in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject in need thereof.

2. Use of:



(i) compound 1: , or a pharmaceutically acceptable salt thereof; and



(ii) compound 2: , or a pharmaceutically acceptable salt thereof, and optionally (iii) one or more of osimertinib, cetuximab, encorafenib, gilteritinib, sotorasib, adagrasib, and palbociclib,

in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject in need thereof.

3. The use of claim 1 or 2, wherein compound 2, or a pharmaceutically acceptable salt thereof, is to be administered in an amount that is between about 30 mg/day and about 300 mg/day.

4. The use of claim 1 or 2, wherein the cancer is a mitogen-activated protein kinase (MAPK) pathway driven cancer, a BRAF-driven cancer, HRAS-driven cancer, or a NRAS-driven cancer.

5. The use of claim 1 or 2, wherein the cancer comprises at least one cancer cell driven by deregulated ERK.

6. The use of claim 1 or 2, wherein the cancer has at least one mutation in RAS, RAF, or MEK.
7. The use of claim 1 or 2, wherein the cancer has a G12C KRAS mutation;
a G12D KRAS mutation;
a G12S KRAS mutation;
a G12V KRAS mutation;
a G13D KRAS mutation;
a Q16H KRAS mutation;
a Q16K KRAS mutation; or
a Q61R NRAS mutation.
8. The use of claim 1 or 2, wherein the cancer is a BRAF V600E or V600K mutant tumor.
9. The use of claim 1 or 2, wherein the cancer is a MAPKm/MAPKi-naïve pancreatic cancer or PDAC.
10. The use of claim 1 or 2, wherein the cancer comprises one or more EGFR mutation selected from the group consisting of EGFR gene copy gain, EGFR gene amplification, chromosome 7 polysomy, EGFR L858R, EGFR exon 19 deletion, EGFR exon insertions, EGFR L861Q, EGFR G719C, EGFR G719S, EGFR G719A, EGFR V765A, EGFR T783A, exon 20 insertion, EGFR splice variant, EGFR A289D, EGFR A289T, EGFR A289V, EGFR G598A, EGFR G598V, EGFR T790M, and EGFR C797S.
11. The use of claim 1 or 2, wherein the cancer is a liquid tumor.
12. The use of claim 11, wherein the liquid tumor is leukemia.
13. The use of claim 11, wherein the leukemia is acute myeloid leukemia (AML).
14. The use of claim 13, wherein the AML is relapsed and/or refractory AML.
15. The use of claim 13, wherein the AML is a FLT3 mutant AML.
16. The use of claim 1 or 2, wherein the cancer is a solid tumor.
17. The use of claim 1 or 2, wherein the cancer is non-small cell lung cancer (NSCLC), melanoma, pancreatic cancer, salivary gland tumor, thyroid cancer, colorectal cancer (CRC), or esophageal cancer.
18. The use of claim 17, wherein the NSCLC is an EGFR mutant, a G12C, G12D, G12S, G12V, G12A, G13D, Q61H, or Q61K KRAS mutant which is optionally KRAS-treated, an NRAS Q61R mutant which is optionally NRAS-treated and wherein the NSCLC is optionally MAPKm/MAPKi-naïve or BRAFi-treated V600 mutant NSCLC.
19. The use of claim 1 or 2, wherein the cancer is pancreatic cancer.
20. The use of claim 1 or 2, wherein the cancer is a MAPKm/MAPKi-naïve pancreatic cancer.
21. The use of claim 20, wherein the pancreatic cancer is pancreatic ductal adenocarcinoma (PDAC).
22. The use of claim 1 or 2, wherein the cancer is melanoma.
23. The use of claim 22, wherein the melanoma has an NF1 Loss of Function (NF1-LoF) mutation.
24. The use of claim 22, wherein the melanoma is a BRAF V600E or V600K mutant tumor.
25. The use of claim 22, wherein the cancer is a BRAFi-treated V600 melanoma.

26. The use of claim 1 or 2, wherein the cancer is colorectal cancer (CRC).

27. The use of claim 26, wherein the CRC is a BRAF V600E mutant, a G12C, G12D, G12S, G12V, G13D, Q61H, or Q61K mutant, or Q61R NRAS mutant CRC.

28. The use of claim 1 or 2, wherein the cancer is esophageal cancer.

29. The use of claim 1 or 2, wherein compound 1, or a pharmaceutically acceptable salt thereof, is to be administered in an amount that is between about 25 mg/day and about 300 mg/day.

30. The use of claim 1 or 2, wherein compound 1, or a pharmaceutically acceptable salt thereof, is to be administered once a day (QD), twice a day (BID), three times a day (TID), once a week, or twice a week.

31. The use of claim 1 or 2, wherein the medicament further comprises an additional MAPK pathway inhibitor selected from a KRAS inhibitor, NRAS inhibitor, HRAS inhibitor, PDGFRA inhibitor, PDGFRB inhibitor, MET inhibitor, FGFR inhibitor, ALK inhibitor, ROS1 inhibitor, TRKA inhibitor, TRKB inhibitor, TRKC inhibitor, EGFR inhibitor, IGFR1R inhibitor, GRB2 inhibitor, SOS inhibitor, ARAF inhibitor, BRAF inhibitor, RAF1 inhibitor, MEK1 inhibitor, MEK2 inhibitor, c-Mycv, CDK4/6, inhibitor CDK2 inhibitor, FLT3 inhibitor, and ERK1/2 inhibitor, wherein the medicament is to be administered.

32. The use of claim 31, wherein the additional MAPK pathway inhibitor is adagrasib, afatinib, ASTX029, binimetinib, cetuximab, cobimetinib, dabrafenib, dacomitinib, encorafenib, erlotinib, gefitinib, gilteritinib, lapatinib, LTT462, LY3214996, necitumumab, neratinib, nimotuzumab, osimertinib, panitumumab, selumetinib, sotorasib, trametinib, ulixertinib, vandetanib, or vemurafenib.