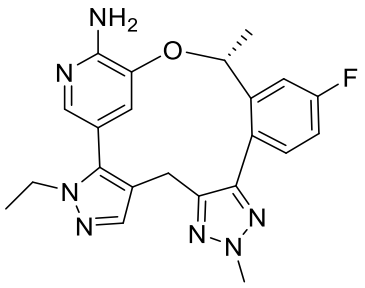
WHAT IS CLAIMED IS:

1. Use of Compound 1:



1,

or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a solid tumor in a patient.

2. The use of claim 1, wherein the solid tumor is advanced solid tumor.

3. The use of claim 2, wherein the advanced solid tumor is relapsed after, refractory to, or resistant to the prior treatment by a tyrosine kinase inhibitor (TKI).

4. The use of any one of claims 1 to 3, wherein the solid tumor is non-small cell lung cancer (NSCLC).

5. The use of any one of claims 1 to 4, wherein the solid tumor is metastatic.

6. The use of claim 5, wherein the solid tumor is CNS metastatic.

7. The use of any one of claims 1 to 6, wherein the solid tumor is ROS1 positive.

8. The use of any one of claims 1 to 6, wherein the solid tumor comprises a ROS1 mutation.

9. The use of claim 8, wherein the ROS1 mutation is one or more mutations selected from G2032R, S1986F, L1951R, L1982F, S9186F, F2004C, F2004V, L2026M, D2033N, and G2101A.

10. The use of any one of claims 1 to 9, wherein the solid tumor comprises a ROS1 fusion.

11. The use of any one of claims 1 to 10, wherein the solid tumor is ALK positive (e.g. ALK fusion) or LTK positive.

12. The use of any one of claims 1 to 11, wherein:

(a) the patient is naïve to tyrosine kinase inhibitor (TKI) therapy;

(b) the patient has been treated with one prior TKI therapy;

(c) the patient has been treated with at least one prior TKI therapy; or

(d) the patient has been treated with at least two prior TKI therapies;

optionally wherein the TKI is ROS1 TKI; or

optionally wherein the prior TKI therapy is one or more selected from the group consisting of crizotinib, ceritinib, alectinib, brigatinib, lorlatinib, entrectinib, repotrectinib, cabozantinib, foretinib, merestinib, taletrectinib, masitinib, and ensartinib.

13. The use of any one of claims 1 to 12, wherein:

(a) the patient has not been treated with prior platinum-based chemotherapy;

(b) the patient has been treated with up to one prior platinum-based chemotherapy;

(c) the patient has been treated with one prior platinum-based chemotherapy;

(d) the patient has not been treated with immunotherapy;

(e) the patient has been treated with immunotherapy;

(f) the patient has not been treated with chemotherapy;

(g) the patient has been treated with at least one prior line of chemotherapy;

(h) the patient has been treated with at least two prior lines of chemotherapy;

(i) the patient has been treated with at least three prior lines of anticancer therapy; or

(j) the patient has been treated with at least two prior lines of anticancer therapy selected from the group consisting of ROS1 TKI (*e.g.*, investigational ROS1 TKI, crizotinib, lorlatinib, entrectinib, repotrectinib, and taletrectinib) and chemotherapy.

14. The use of any one of claims 1 to 13, wherein:

(a) the patient has been treated with at least one line of ROS1 TKI and one line of chemotherapy;

(b) the patient has been treated with at least two lines of ROS1 TKI and one line of chemotherapy;

(c) the patient has been treated with at least three lines of ROS1 TKI and one line of chemotherapy;

(d) the patient has been treated with at least two lines of chemotherapy;

(e) the patient has been treated with at least one line of ROS1 TKI and two lines of chemotherapy;

(f) the patient has been treated with at least two lines of ROS1 TKI and two lines of chemotherapy; or

(g) the patient has been treated with at least three lines of ROS1 TKI and two lines of chemotherapy;

optionally wherein the ROS1 TKI is crizotinib, entrectinib, lorlatinib, or repotrectinib; or

optionally wherein the patient has been treated with lorlatinib and repotrectinib.

15. The use of any one of claims 1 to 14, wherein

a. the solid tumor is advanced or metastatic ROS1-positive solid tumor, and the patient has been treated with at least one prior ROS1 TKI therapy;

b. the solid tumor is advanced or metastatic ROS1-positive NSCLC, and the patient is naïve to TKI therapy and has been treated with up to one prior platinum-based chemotherapy with or without immunotherapy;

c. the solid tumor is advanced or metastatic ROS1-positive NSCLC, and the patient has been treated with one prior ROS1 TKI therapy and has not been treated with prior platinum-based chemotherapy or immunotherapy;

d. the solid tumor is advanced or metastatic ROS1-positive NSCLC, and the patient has been treated with one prior ROS1 TKI therapy and one prior platinum-based chemotherapy with or without immunotherapy;

e. the solid tumor is advanced or metastatic ROS1-positive NSCLC, and the patient has been treated with at least two prior ROS1 TKI therapies and up to one prior platinum-based chemotherapy with or without immunotherapy; or

f. the solid tumor is advanced or metastatic ROS1-positive solid tumor, and the patient has progressed on a prior therapy,

optionally wherein the prior ROS1 TKI is investigational ROS1 TKI, crizotinib, lorlatinib, entrectinib, repotrectinib, and taletrectinib.

16. The use of any one of claims 1 to 15, wherein Compound 1 is to be administered to the patient for at least one treatment cycle, optionally wherein one treatment cycle is at least 7 days, at least 14 days, at least 21 days, or at least 28 days.

17. The use of any one of claims 1 to 16, wherein:

a. the patient does not experience a Grade 4 adverse event (*e.g.*, TRAE) after the administration of Compound 1;

b. the patient does not experience a Grade 3 adverse event (*e.g.*, TRAE) after the administration of Compound 1;

c. the patient does not experience a Grade 2 adverse event (*e.g.*, TRAE) after the administration of Compound 1;

d. the patient does not experience a Grade 1 adverse event (*e.g.*, TRAE) after the administration of Compound 1; and/or

e. the patient experiences at most a Grade 1 adverse event (*e.g.*, TRAE) after the administration of Compound 1,

optionally wherein the Grade 1 adverse event is fatigue, myalgia or nausea.

18. The use of any one of claims 1 to 17, wherein the patient does not experience a CNS adverse event after the administration of Compound 1, optionally wherein the CNS adverse event is one or more selected from the group consisting of dizziness, ataxia, gait disturbance, paraesthesia, weight gain, hyperphagia, paresthesias, abnormal movement, cognitive changes, speech effects (e.g, dysarthria, slow speech, or speech disorder), mood disorder (e.g., irritability, anxiety, depression, affect lability, personality change, mood swings, affective disorder, aggression, agitation, mood altered, depressed mood, euphoric mood, or mania), and cognitive disorder (e.g., memory impairment, cognitive disorder, amnesia, confusion, disturbance in

attention, delirium, mental impairment, attention deficit/hyperactivity disorder, dementia, sleep disturbance, or reading disorder).

19. The use of any one of claims 1 to 18, wherein the patient is a patient population, and:

a. less than 30% of the patient population experiences a Grade 1 TRAE after administration of Compound 1;

b. less than 20% of the patient population experiences a Grade 2 TRAE after administration of Compound 1; or

c. the patient population experiences no Grade 3 or Grade 4 TRAE after administration of Compound 1.

20. The use of any one of claims 1 to 19, wherein

a. the patient has a partial or complete response after one or more cycles of treatment; or

b. the patient has reached stable disease after one or more cycles of treatment.

21. The use of any one of claims 1 to 20, wherein the patient has brain metastases, and optionally experiences no intracranial progression after at least one treatment cycle.

22. The use of any one of claims 1 to 21, wherein the patient has at least about 5% to about 100% reduction of ROS1 allele variant in circulating tumor DNA after at least one treatment cycle, or has undetectable ROS1 allele variant in circulating tumor DNA after at least one treatment cycle.

23. The use of any one of claims 1 to 22, wherein administration of the compound provides:

a. the area under the curve from 0 to 24 hours after administration (AUC_{0-24}) of the compound in a range of (80% to 125% of 20 ng*h/mL) to (80% to 125% of 500 ng*h/mL) for every mg of Compound 1 to be administered;

b. the $AUC_{last, unbound}$ of the compound in a range of from about 10 to about 80 ng*h/mL for every mg of Compound 1 to be administered;

c. the AUC_{tau} of the compound in a range of about 50 to about 150 ng*h/mL for every mg of Compound 1 to be administered;

d. the AUC_{inf} of the compound in a range of about 50 to about 250 ng*h/mL for every mg of Compound 1 to be administered;

e. the maximum plasma concentration (C_{max}) of the compound in a range of about 2 to about 50 ng/mL for every mg of Compound 1 to be administered;

f. the minimum plasma concentration to be reached by Compound 1 during the time interval between administration of two doses (C_{min}) in a range of about 50 to about 350 ng/mL;

g. the unbound maximum plasma concentration ($C_{max, unbound}$) of the compound in a range of about 30 ng/mL to about 400 ng/mL;

h. the T_{max} of the compound after the administration in a range of about 0.25h to about 5h, or about 0.7h to about 1.3h;

i. the $t_{1/2}$ of the compound after the administration in a range of about 2h to about 50h, or about 10h to about 24h; and/or

j. the dose plasma concentration of the compound at least 10%, 20%, 30%, 40%, or 50% higher than the IC_{50} of the compound against ROS1 G2032R mutant during at least 70%, 80%, 90%, 95%, 97%, 98%, or 99% of about 24 hours immediately following the administration.

24. Use of Compound 1 in the manufacture of a medicament for reducing a lesion in a subject having a ROS1-positive solid tumor, wherein Compound 1 is to be administered once daily for one or more days after a first radiological measurement of the size of the lesion has been obtained, and

wherein a second radiological measurement of the size of the lesion is to be obtained after Compound 1 is administered; and
wherein the second measurement is at most 100%, at most 90%, at most 80%, at most 70%, at most 60%, or at most 50% of the first measurement.

25. The use of any one of claims 1 to 24, wherein the compound is to be administered at an amount of from about 5 mg to about 500 mg (by weight of Compound 1 free base) once daily or twice daily (BID), optionally wherein the compound is to be administered at an amount of about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 75 mg, about 100 mg, about 125 mg, or about 150 mg (by weight of free base Compound 1) once daily or twice daily (BID).

26. The use of any one of claims 1 to 25, wherein the compound is to be administered in the absence of a sensitive substrate of CYP3A4, optionally wherein the sensitive substrates of CYP3A4 comprise one or more of buspirone, everolimus, lovastatin, midazolam, simvastatin, triazolam, maraviroc, conivaptan, and darifenacin.

27. The use of any one of claims 1 to 26, wherein the patient experiences:

a. reduced levels of one or more of pROS1, ROS1, pAKT, and pERK, after administration of the compound;

b. reduced expression level of one or more MAP kinase pathway genes in tumor, after administration of the compound; and/or

c. reduced expression level of one or more MAP kinase pathway genes in solid tumor, after administration of the compound, optionally wherein the one or more MAP kinase pathway genes are selected from the group consisting of *DUSP6*, *FOS*, *IL1R1*, and *SPRY4*.

28. The use of any one of claims 1 to 27, wherein the compound is Compound 1 free base, optionally wherein the compound to be administered is a solid form of Compound 1 characterized by an XRPD pattern comprising peaks at approximately 10.7, 15.0, and 21.2º 2θ (±0.2º).

29. The use of any one of claims 1 to 28, wherein the compound is to be administered as a pharmaceutical composition comprising Compound 1, or a stereoisomer, or a mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, and a diluent, a binder, a disintegrant, and a lubricant,

optionally wherein the diluent is mannitol, the binder is a mixture of HPC and SMCC, the disintegrant is sodium starch glycolate (SSG), and the lubricant is magnesium stearate.