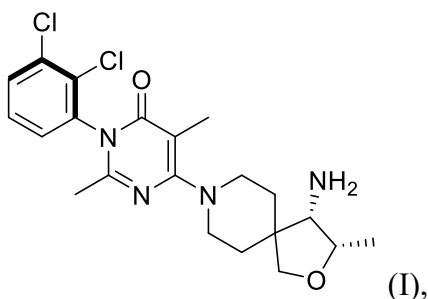


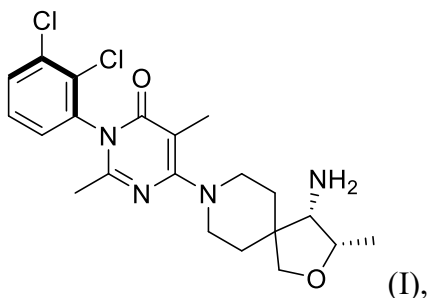
CLAIMS

1 1. Use of a compound represented by formula (I):



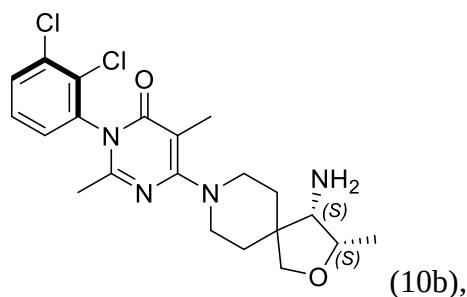
2
3 or a pharmaceutically acceptable salt, hydrate, solvate, stereoisomer, conformational isomer,
4 tautomer, or a combination thereof, in the preparation of a medicament for treating cancer in a
5 subject, wherein the subject has (i) one or more mutations in MAPK pathway, provided that the
6 one or more mutations in MAPK pathway are other than a BRAF mutation comprising V600X
7 mutation, and/or (ii) one or more mutations in *PTPN11*.

1 2. Use of a compound represented by formula (I):



2
3 or a pharmaceutically acceptable salt, hydrate, solvate, stereoisomer, conformational isomer,
4 tautomer, or a combination thereof, in the preparation of a medicament for treating a solid tumor
5 in a subject, wherein the subject has (i) one or more mutations in MAPK pathway, provided that
6 the one or more mutations in MAPK pathway are other than a BRAF mutation comprising
7 V600X mutation, and/or (ii) one or more mutations in *PTPN11*.

1 3. The use of claim 1 or 2, wherein the compound of formula (I) is
2 represented by formula (10b):



having the name of 6-((3S,4S)-4-amino-3-methyl-2-oxa-8-azaspiro[4.5]decan-8-yl)-3-(*R_a*)-(2,3-dichlorophenyl)-2,5-dimethylpyrimidin-4(3*H*)-one.

4. The use of any one of claims **1** to **3**, wherein the subject has a KRAS mutation comprising a KRAS G12C mutation.

5. The use of any one of claims **1** to **4**, wherein the cancer or solid tumor is an advanced or metastatic KRAS G12C-positive solid tumor.

6. The use of claim **5**, wherein the solid tumor is an advanced or metastatic KRAS G12C-positive non-small cell lung cancer (NSCLC).

7. The use of claim **5**, wherein the solid tumor is an advanced or metastatic KRAS G12C-positive solid tumor, provided that the solid tumor is other than non-small cell lung cancer (NSCLC).

8. The use of any one of claims **1** to **3**, wherein the cancer or solid tumor is an advanced or metastatic KRAS mutant solid tumor.

9. The use of any one of claims **1** to **8**, wherein the subject has one or more mutations in MAPK pathway selected from the group consisting of one or more mutations in KRAS, NRAS, HRAS, CRAF, BRAF, NRAF, MAPK/ERK, MAPKK/MEK, NF1, IGFR, EGFR, PDGFR, VEGFR, FGFR, CCKR, NGFR, EphR, AXL, KEAP1, TIE receptor, RYK receptor, DDR receptor, RET receptor, ROS receptor, LTK receptor, ROR receptor, MuSK receptor, and a combination thereof.

10. The use of any one of claims **1** to **3** and **9**, wherein the cancer or solid tumor is an advanced or metastatic NF1 LOF solid tumor.

1 **11.** The use of any one of claims **1** to **3** and **9**, wherein the cancer or solid
2 tumor is an advanced or metastatic BRAF class II/III mutant solid tumor.

1 **12.** The use of any one of claims **1** to **3**, wherein the cancer or solid tumor is
2 chordoma or notochordal sarcoma.

1 **13.** The use of any one of claims **1** to **9**, wherein the subject has an EGFR
2 mutation comprising an EGFR exon 19 deletion, exon 20 insertion, L858X mutation, T790X
3 mutation, C797X mutation, G719X mutation, L861X mutation, S768X mutation, E709X
4 mutation, or any combination thereof.

1 **14.** The use of any one of claims **1** to **3** and **13**, wherein the cancer or solid
2 tumor is an advanced or metastatic EGFR-positive solid tumor.

1 **15.** The use of claim **14**, wherein the solid tumor is an advanced or metastatic
2 EGFR-positive non-small cell lung cancer (NSCLC), optionally progressed on a standard of care
3 EGFR tyrosine kinase inhibitor (TKI) therapy.

1 **16.** The use of any one of claims **1** to **15**, wherein a standard of care or
2 curative therapy is unavailable for treating the cancer or solid tumor.

1 **17.** The use of any one of claims **1** to **16**, wherein the subject has adequate
2 organ functions comprising adequate hematological, renal, hepatic, and coagulating functions.

1 **18.** The use of any one of claims **1** to **17**, wherein:
2 a) the subject is not previously treated with a cancer therapy comprising a chemotherapy,
3 a hormone therapy, an immunotherapy or biological therapy, a targeted therapy,
4 or a combination thereof; or
5 b) the subject discontinues a cancer therapy comprising a chemotherapy, a hormone
6 therapy, an immunotherapy or biological therapy, a targeted therapy, or a
7 combination thereof for a period of at least about three weeks or five (5) half-lives
8 of an agent used in the cancer therapy, whichever is longer prior to initiation of
9 the treatment with the compound of formula (I) or (10b).

1 **19.** The use of any one of claims **1** to **18**, wherein the subject does not have
2 one or more additional activating mutations in PTPN11 (SHP2), MEK, or RAS Q61.

1 **20.** The use of any one of claims **1** to **19**, wherein the subject does not have an
2 additional malignancy that is progressing or requires an active treatment, a primary central
3 nervous system (CNS) tumor, an active CNS metastasis, and/or a carcinomatous meningitis.

1 **21.** The use of any one of claims **1** to **20**, wherein the subject is not previously
2 treated with a SHP2 inhibitor, provided that the SHP2 inhibitor is other than the compound of
3 formula (I) or (10b).

1 **22.** The use of any one of claims **1** to **21**, wherein the treating comprises one
2 or more treatment cycles; and the compound of formula (I) or (10b) is to be administered and the
3 administration comprises a dose escalation or de-escalation after a previous treatment cycle,
4 wherein the dose escalation or de-escalation is determined by a dose-limiting toxicity (DLT)
5 assessment.

1 **23.** The use of claim **22**, wherein the administration of the compound of
2 formula (I) or (10b) comprises 1 to 6 dose escalations, optionally 1 to 2 dose de-escalations.

1 **24.** The use of claim **22** or **23**, wherein each of one or more treatment cycles
2 has a duration of about 28 days and the compound of formula (I) or (10b) is to be administered
3 daily.

1 **25.** The use of any one of claims **1** to **24**, wherein the compound is to be
2 administered in a therapeutically effective amount, which is a total daily dosage of from about 10
3 mg to about 2000 mg, from about 50 mg to about 2000 mg, from about 80 mg to about 2000 mg,
4 from about 80 mg to about 1000 mg, from about 80 mg to about 700 mg, from about 80 mg to
5 about 550 mg, from about 80 mg to about 450 mg, from about 80 mg to about 400 mg, from
6 about 80 mg to about 250 mg, or from about 80 mg to about 150 mg of the compound of formula
7 (I) or (10b), on a salt-free and anhydrous basis.

1 **26.** The use of claim **25**, wherein the therapeutically effective amount is a total
2 daily dosage of from about 80 mg to about 700 mg, from about 80 mg to about 550 mg, from
3 about 80 mg to about 450 mg, from about 80 mg to about 400 mg, from about 80 mg to about
4 250 mg, or from about 80 mg to about 150 mg of the compound of formula (I) or (10b), on a
5 salt-free and anhydrous basis.

1 **27.** The use of claim **25** or **26**, wherein the therapeutically effective amount is
2 a total daily dosage of about 80 mg, about 150 mg, about 250 mg, about 400 mg, about 450 mg,
3 about 550 mg, or about 700 mg of the compound of formula (I) or (10b), on a salt-free and
4 anhydrous basis.

1 **28.** The use of any one of claims **25** to **27**, wherein the therapeutically
2 effective amount is a total daily dosage of about 80 mg of the compound of formula (I) or (10b),
3 on a salt-free and anhydrous basis.

1 **29.** The use of any one of claims **25** to **27**, wherein the therapeutically
2 effective amount is a total daily dosage of about 150 mg of the compound of formula (I) or
3 (10b), on a salt-free and anhydrous basis.

1 **30.** The use of any one of claims **25** to **27**, wherein the therapeutically
2 effective amount is a total daily dosage of about 250 mg of the compound of formula (I) or
3 (10b), on a salt-free and anhydrous basis.

1 **31.** The use of any one of claims **25** to **27**, wherein the therapeutically
2 effective amount is a total daily dosage of about 400 mg of the compound of formula (I) or
3 (10b), on a salt-free and anhydrous basis.

1 **32.** The use of any one of claims **25** to **27**, wherein the therapeutically
2 effective amount is a total daily dosage of about 450 mg of the compound of formula (I) or
3 (10b), on a salt-free and anhydrous basis.

1 **33.** The use of any one of claims **25** to **27**, wherein the therapeutically
2 effective amount is a total daily dosage of about 550 mg of the compound of formula (I) or
3 (10b), on a salt-free and anhydrous basis.

1 **34.** The use of any one of claims **25** to **27**, wherein the therapeutically
2 effective amount is a total daily dosage of about 700 mg of the compound of formula (I) or
3 (10b), on a salt-free and anhydrous basis.

1 **35.** The use of any one of claims **1** to **34**, wherein the compound of formula (I)
2 or (10b) is to be administered orally.

1 **36.** The use of any one of claims **1** to **35**, wherein the compound of formula (I)
2 or (10b) is to be administered once, twice, three times, or four times daily.

1 **37.** The use of claim **36**, wherein the compound of formula (I) or (10b) is to be
2 administered once daily.

1 **38.** The use of any one of claims **1** to **37**, wherein the compound of formula (I)
2 or (10b) is to be administered to the subject without food, at least about 8 hours prior to the
3 administration and at least about 2 hours post the administration.

1 **39.** The use of any one of claims **1** to **38**, wherein a maximum tolerate dose
2 (MTD) and/or a dose-limiting toxicity (DLT) are determined according to the dose-limiting
3 toxicity (DLT) assessment.

1 **40.** The use of any one of claims **1** to **39**, wherein the therapeutically effective
2 amount of formula (I) or (10b) reduces a volume of the cancer or solid tumor at least about 10%,
3 about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, or about
4 90%.

1 **41.** The use of any one of claims **1** to **39**, wherein the therapeutically effective
2 amount of formula (I) or (10b) stabilize the cancer or solid tumor.

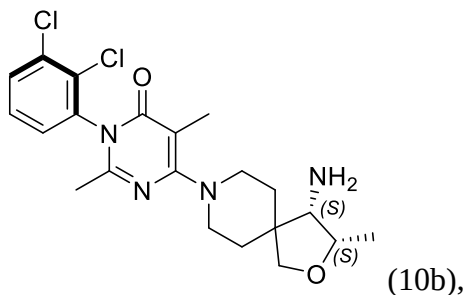
1 **42.** The use of claim **40** or **41**, wherein the cancer or solid tumor is reduced or
2 stabilized for a period of at least about one month.

1 **43.** The use of any one of claims **40** to **42**, wherein the cancer or solid tumor is
2 reduced or stabilized for a period of from about 1 to about 12 months, from about 1 to about 6
3 months, from about 1 to about 3 months, or from about 1 to about 2 months.

1 **44.** The use of any one of claims **1** to **43**, wherein the subject is further
2 evaluated according to one or more parameters of Table 3, Table 4, and Table 5 comprising
3 plasma pharmacokinetic parameters and/or pharmacodynamic parameters.

1 **45.** The use of any one of claims **1** to **44**, wherein the subject is further
2 evaluated for one or more biomarkers that correlate to an antitumor response.

1 **46.** Use of a compound represented by formula (10b):



2 or a tautomer thereof, in the preparation of a medicament for the treatment of a tumor in a
3 subject, wherein the subject has (i) one or more mutations in MAPK pathway, provided that the
4 one or more mutations in MAPK pathway are other than a BRAF mutation comprising V600X
5 mutation, and/or (ii) one or more mutations in *PTPN11*.

1 **47.** The use of claim **46**, wherein the tumor is an advanced or metastatic
2 KRAS G12C-positive non-small cell lung cancer (NSCLC).

1 **48.** The use of claim **46**, wherein the tumor is an advanced or metastatic
2 KRAS G12C-positive solid tumor, provided that the solid tumor is other than non-small cell lung
3 cancer (NSCLC).

1 **49.** The use of claim **46**, wherein the tumor is the solid tumor is an advanced
2 or metastatic EGFR-positive non-small cell lung cancer (NSCLC), optionally progressed on a
3 standard of care EGFR tyrosine kinase inhibitor (TKI) therapy.

1 **50.** The use of claim **46**, wherein the tumor is an advanced or metastatic
2 KRAS mutant solid tumor.

1 **51.** The use of claim **46**, wherein the tumor is an advanced or metastatic NF1
2 LOF solid tumor.

1 **52.** The use of claim **46**, wherein the tumor is an advanced or metastatic
2 BRAF class II/III mutant solid tumor.

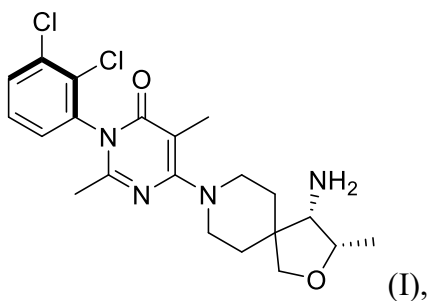
1 **53.** The use of claim **46**, wherein the tumor is chordoma or notochordal
2 sarcoma.

1 **54.** The use of any one of claims **46** to **53**, wherein the compound is to be
2 administered in a therapeutically effective amount, which is a total daily dosage of about 450 mg
3 of the compound of formula (10b), on a salt-free and anhydrous basis.

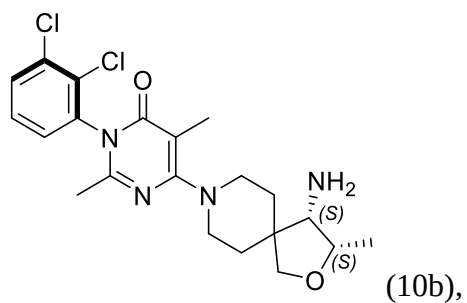
1 **55.** The use of any one of claims **46** to **54**, wherein the compound of formula
2 (10b) is administered once daily.

1 **56.** The use of any one of claims **46** to **55**, wherein the compound of formula
2 (10b) is administered orally.

1 **57.** A kit for treating cancer or a solid tumor in a subject, comprising:
2 a compound represented by formula (I):



3
4 or a pharmaceutically acceptable salt, hydrate, solvate, stereoisomer, conformational
5 isomer, tautomer, or a combination thereof; or
6 a compound represented by formula (10b):



or a tautomer thereof,

together with instruction for effective administration, wherein the subject has (i) one or more mutations in MAPK pathway, provided that the one or more mutations in MAPK pathway are other than a BRAF mutation comprising V600X mutation, and/or (ii) one or more mutations in *PTPN11*