

form (where the entire lining of the joint is involved). Treatment is surgical excision of the tumor. However, it is often difficult to perform a marginal excision for the diffuse form of TGCT resulting in a high recurrence rate. It can be characterized by overexpression of CSF1.

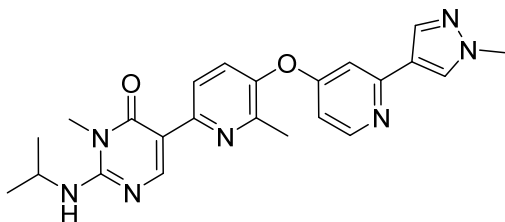
5 [0005] There is a need for selective small-molecule CSF1R inhibitors that are useful in the treatment of disorders associated with the proliferation of TAMs including solid tumors of various cancers and treatment of mesenchymal tumors including TGCT and diffuse-type tenosynovial giant cell tumor (DTGCT).

SUMMARY

10 [0006] Provided herein, in part, are methods of treating disorders such as tenosynovial giant cell tumors and/or or cancers in a patient in need thereof, comprising orally administering to the patient a therapeutically effective amount of the compound 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one or a pharmaceutically acceptable salt thereof.

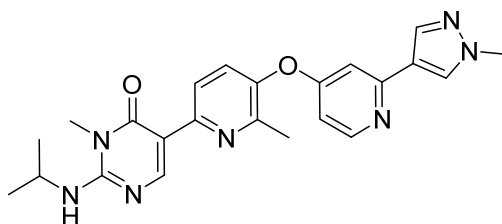
15 [0007] For example, described herein is a method of treating a cancer selected from the group consisting of solid tumors, acute myeloid leukemia, myelodysplastic syndrome, acute lymphocytic leukemia, and chronic lymphocytic leukemia, in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of the compound 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one or a pharmaceutically acceptable salt thereof,
20 wherein administering comprises: administering a loading dose of the compound daily for a first time period; and administering a maintenance dose of the compound once a week, twice a week (also described as biweekly), or three times a week for a second time period.

[0007a] In one aspect of the present disclosure, there is provided a use of a compound
25 represented by:



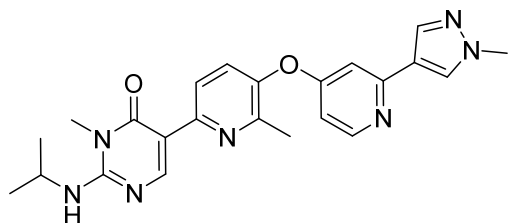
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a tenosynovial giant cell tumor in a patient in need thereof, wherein the compound is to be orally administered to the patient.

[0007b] In another aspect of the present disclosure, there is provided a use of a compound represented by:



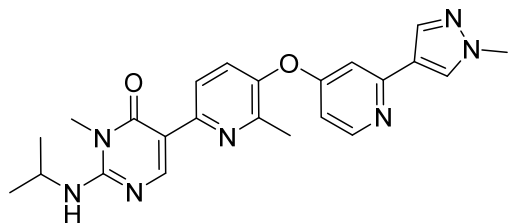
5 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a tenosynovial giant cell tumor in a patient in need thereof, wherein 2 mg to 50 mg of the compound is to be orally administered to the patient twice weekly.

[0007c] In a further aspect of the present disclosure, there is provided Use of a compound represented by:



10 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a tenosynovial giant cell tumor in a patient in need thereof, wherein 30 mg of the compound is to be orally administered to the patient twice weekly.

[0007d] In another aspect of the present disclosure, there is provided a use of a compound represented by:



or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating tumors known to have expression of the receptor colony-stimulating factor 1 receptor (CSF1R) or its ligands, colony stimulating factor-1 (CSF1) or interleukin (IL)-34 in a patient
 5 in need thereof, wherein 2 mg to 60 mg of the compound is to be orally administered to the patient.

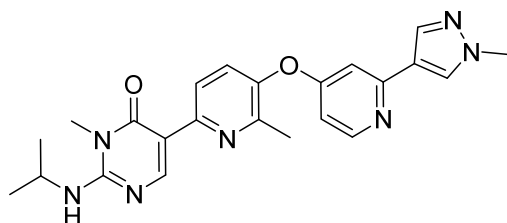
[0008] The disclosure also provides for a method of treating tumors, e.g., GCTTS, PVNS, TGCT or DTGCT, comprising administering to the patient a therapeutically effective amount of the compound 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one or a pharmaceutically acceptable salt
 10 thereof, wherein administering comprises: administering a loading dose of the compound daily for a first time period; and administering a maintenance dose of the compound once a week, twice a week, or three times a week for a second time period.

[0009] A method of inhibiting the proliferation of a cell known to have expression of the receptor colony-stimulating factor 1 receptor (CSF1R) or its ligands, colony-stimulating
 15 factor 1 (CSF1) or interleukin (IL)-34 in a patient in need thereof is also contemplated herein,

CLAIMS

What is claimed is:

1. Use of a compound represented by:

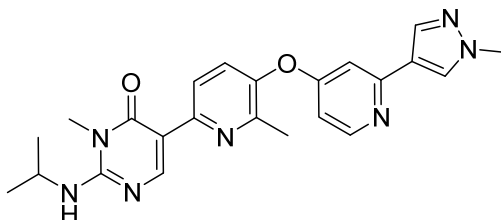


- 5 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a tenosynovial giant cell tumor in a patient in need thereof, wherein the compound is to be orally administered to the patient.
2. The use of claim 1, wherein the tenosynovial giant cell tumor is diffuse-type tenosynovial giant cell tumor.
- 10 3. The use of claim 1, wherein the tumor is benign.
4. The use of any one of claims 1-3, wherein 2 mg to 60 mg of the compound is to be administered to the patient daily, once a week, twice a week, or three times a week.
5. The use of any one of claims 1-3, wherein 10 to 90 mg of the compound is to be administered to the patient daily, once a week, twice a week, or three times a week.
- 15 6. The use of any one of claims 1-3, wherein
a loading dose of the compound is to be administered daily for a first time period;
and
a maintenance dose of the compound is to be administered daily, twice weekly, or three times a week for a second time period.
- 20 7. The use of claim 6, wherein the loading dose is 10 to 80mg/day.
8. The use of claim 6 or 7 wherein the loading dose is 20 to 60mg/day.

9. The use of any one of claims 6-8, wherein the loading dose is 20mg, 30mg/day, 40mg/day, 50mg/day or 60mg/day.
10. The use of any one of claims 6-9, wherein the maintenance dose is 2mg to 60mg.
11. The use of any one of claims 6-10, wherein the maintenance dose is 2mg, 10 mg, 20mg, 25mg, 30mg, 40mg or 50mg each administered twice or three times a week.
12. The use of any one of claims 6-11, wherein the first time period is one or two weeks.
13. The use of any one of claims 6-12, wherein the first time period is 4 days, 5 days, 6 days, or 10 days.
14. The use of any one of claims 6-13, wherein the second time period is one month to two months, three months or more.
15. The use of any one of claims 6-14, wherein the second time period is one month to nine months or more.
16. The use of any one of claims 6-14, wherein an additional loading dose is to be further administered during a third time period.
17. The use of claim 16, wherein an additional maintenance dose is to be further administered during a fourth time period.
18. The use of claim 15 or 16, wherein the third and/or fourth time period occurs after the first and second time period.
19. The use of any one of claims 1-17, wherein after 1 month or more of administration, the patient has an improved tumor response as measured by CT, MRI and/or RECIST.
20. The use of any one of claims 1-18, wherein the compound is to be administered for 1 month or more, and after 1 month or more of administration, the patient has an improved range of motion.
21. The use of any one of claims 1-19, wherein the compound is to be administered for 1 month or more, and after 1 month or more of administration, the patient has reduced macrophage infiltration in the affected joint and/or circulating chemokine/cytokines associated with inflammation as compared to the amounts before administration.

22. The use of any one of claims 6-21, wherein the compound is to be administered, and wherein the size of the tenosynovial giant cell tumor decreases to 90% to 10% of its size prior to administering.

23. Use of a compound represented by:



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or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a tenosynovial giant cell tumor in a patient in need thereof, wherein 2 mg to 50 mg of the compound is to be orally administered to the patient twice weekly.

24. The use of claim 23, wherein 5 mg to 30 mg of the compound is to be administered to the patient twice weekly.

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25. The use of claim 23 or 24, wherein 20 mg of the compound is to be administered to the patient twice weekly.

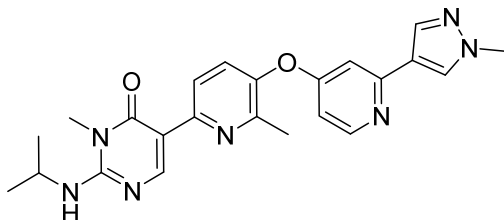
26. The use of claim 23 or 24, wherein 14 mg of the compound is to be administered to the patient twice weekly.

27. The use of any one of claims 23-26, wherein the tenosynovial giant cell tumor is a diffuse-type tenosynovial giant cell tumor.

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28. The use of any one of claims 23-27, wherein the tumor is benign.

29. Use of a compound represented by:



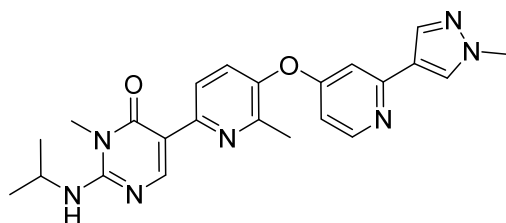
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a tenosynovial giant cell tumor in a patient in need thereof, wherein 30 mg of the compound is to be orally administered to the patient twice weekly.

30. The use of claim 29, wherein the tumor is benign.

5 31. The use of claim 29 or 30, wherein the compound is to be administered to the patient twice weekly for at least 6 months.

32. The use of claim 29 or 30, wherein the compound is to be administered to the patient twice weekly for 1 year.

33. Use of a compound represented by:



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or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating tumors known to have expression of the receptor colony-stimulating factor 1 receptor (CSF1R) or its ligands, colony stimulating factor-1 (CSF1) or interleukin (IL)-34 in a patient in need thereof, wherein 2 mg to 60 mg of the compound is to be orally administered to the patient.

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34. The use of claim 33, wherein 5 mg to 30 mg of the compound is to be administered to the patient twice weekly.

35. The use of claim 33, wherein 30 mg of the compound is to be administered to the patient twice weekly.

20 36. The use of any one of claims 33-35, wherein the tenosynovial giant cell tumor is a diffuse-type tenosynovial giant cell tumor.

37. The use of any one of claims 33-36, wherein the tumor is benign.

38. The use of any one of claims 33-37, wherein expression of CSF1R, CSF1, or IL-34 in the tumor is to be determined from the patient's extracted tumor sample, or patient's extracellular fluid.
39. The use of any one of claims 33-37, wherein expression of CSF1R, CSF1, or IL-34 in the tumor's microenvironment is to be determined from the patient's extracted tumor sample, or patient's extracellular fluid.
40. The use any one of claims 1-39, wherein the tenosynovial giant cell tumor is additionally to be surgically treated in the patient.
41. The use of claim 40, wherein the compound is to be administered to the patient as an adjuvant after surgically treating the tenosynovial giant cell tumor in the patient.
42. The use of claim 40, wherein the compound is to be administered to the patient as a neo-adjuvant prior to surgically treating the tenosynovial giant cell tumor in the patient.
43. The use of any one of claims 1-42, wherein after 1 month or more of administration, the patient has: (i) an improved tumor response as measured by CT, MRI and/or RECIST; and/or (ii) an improved range of motion; and/or (iii) reduced macrophage infiltration in the affected joint and/or circulating chemokine/cytokines associated with inflammation as compared to the amounts before administration.
44. The use of claim 43, wherein the size of the tenosynovial giant cell tumor decreases to 90% to 10% of its size prior to administering.
45. The use of claim 29 or 30, wherein the compound is to be administered to the patient twice weekly for at least 3 months.
46. The use of claim 29 or 30, wherein the compound is to be administered to the patient twice weekly for at least 1 month.