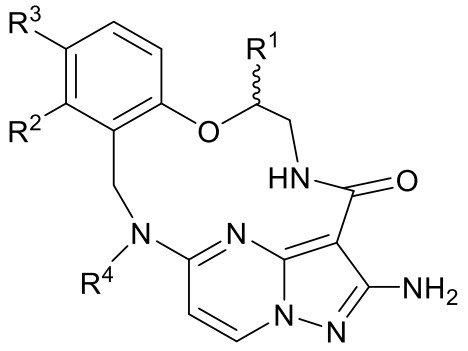
lymphocytes under normal physiological conditions. Activation of Fyn is observed in various cancers, including melanoma, glioblastoma, squamous cell carcinoma, prostate and breast cancers. (Elias D., et al. *Pharmacological Research* **2015**, *100*, 250-254) Fyn was upregulated in tamoxifen-resistant breast cancer cell lines and plays a key role in the resistance mechanism. Peripheral T-cell lymphomas (PTCLs) are a heterogeneous group of aggressive non Hodgkin lymphomas with poor prognosis. FYN activating mutations were found in PTCL, and promoted the growth of cells transformed via expression of activated FYN mutant alleles. SRC kinase inhibitors may play important roles in the treatment of PTCLs. (Couronne L, et al. *Blood* 2013, 122, 811).

**[007]** It is desirable to prepare compounds that have activity against disease-driving kinase inhibitors, especially compounds that have activity against genetically altered MET, SCR and CSF1R. New compounds with polypharmacology profiles are also desired for targeting the primary oncogene drivers and their acquired resistance mechanisms including secondary mutations, bypass signaling, EMT, cancer stemness, and metastasis.

SUMMARY

**[007a]** In an aspect, there is provided a use of a compound in the preparation of a medicament for treating cancer in a patient, wherein the compound is of formula




wherein

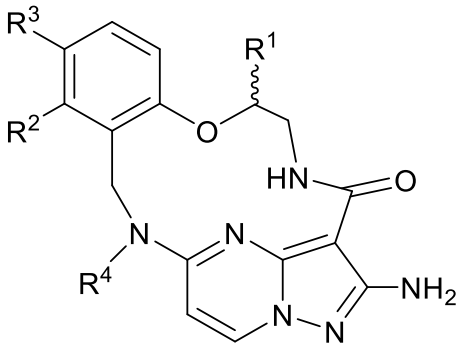
$R^1$ is H, deuterium, or $C_1$-$C_6$ alkyl;

$R^2$ is chloro or -CN;

$R^3$ is H, deuterium, or fluoro;

$R^4$ is H or $C_1$-$C_6$ alkyl, wherein each hydrogen atom in $C_1$-$C_6$ alkyl is independently optionally substituted by deuterium, fluoro, chloro, bromo, -OH, -CN, -O$C_1$-$C_6$ alkyl, -$NH_2$, -NH($C_1$-$C_6$ alkyl), -N($C_1$-$C_6$ alkyl)$_2$, or $C_3$-$C_7$ cycloalkyl, or a pharmaceutically acceptable salt thereof.

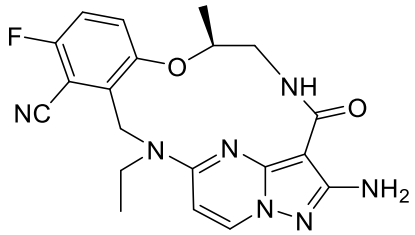
**[008]** Compounds that inhibit MET, SRC, and CSF1R gene products have been discovered. Compounds of the formula I



I

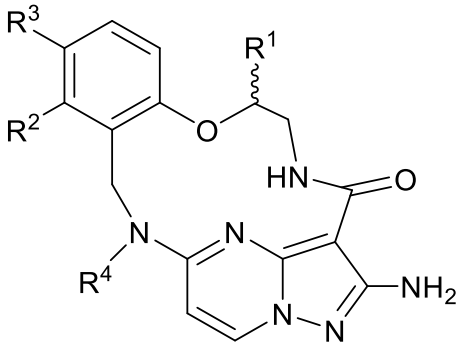
wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein have been shown to have activity against wild-type and mutant MET, SRC, and CSF1R.

**[009]** One such compound is (7*S*)-3-amino-14-ethyl-11-fluoro-7-methyl-4-oxo-4,5,6,7,13,14-hexahydro-1,15-ethenopyrazolo[4,3-*f*][1,4,8,10]benzoxatriazacyclotridecine-12-carbonitrile (also herein referred to as "Compound 1"), represented by the formula



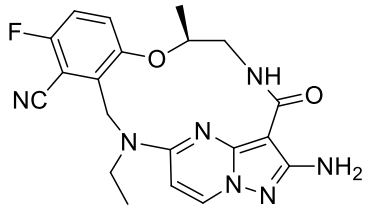

has been shown to be a potent small-molecule kinase inhibitor showing activity against wild-type and mutant wild-type and mutant MET, SRC, and CSF1R. Compound 1 has properties, including anti-tumor properties, which are pharmacologically mediated through inhibition of receptor and non-receptor tyrosine kinases. Compounds of the formula I, in particular, Compound 1, are disclosed in International Patent Publication No. WO2019/023417, which is incorporated herein by reference in its entirety.

**[010]** In one example~~aspect~~, the present disclosure provide a method of treating disease, such as cancer, in a mammal, in particular a human patient comprising, administering to the mammal, in particular a human patient, a therapeutically effective amount of a compound that inhibits MET, SRC, and CSF1R, wherein the disease is mediated by a genetically altered MET. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



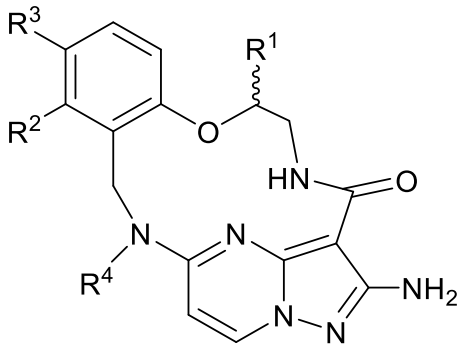

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or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



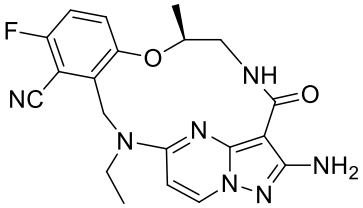
or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the mammal, in particular a human patient, has received prior treatment with one or more therapeutic agents.

**[011]** In another example~~aspect~~, the present disclosure provides a method of treating cancer in a patient previously shown to express a genetically altered MET comprising, administering to the patient a therapeutically effective amount of a compound that inhibits MET, SRC, and CSF1R. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



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or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula

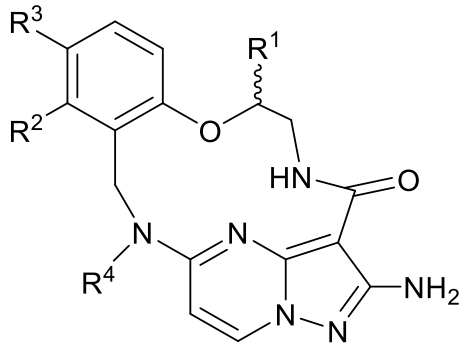


or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

**[012]** In another example~~aspect~~, the present disclosure provides a method of treating cancer in a patient comprising;

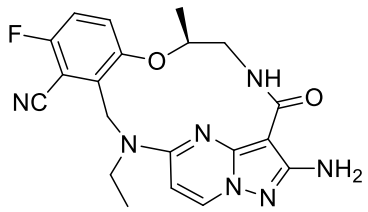
i. identifying a genetically altered MET in the patient, and

ii. administering to the patient a therapeutically effective amount of a compound that inhibits MET, SRC, and CSF1R. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



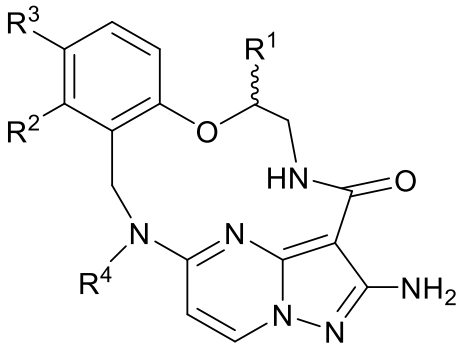
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or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



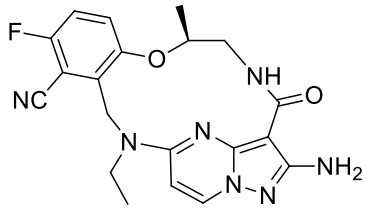
or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

**[013]** In another example~~aspect~~, the present disclosure provides a method of identifying a patient for treatment with a compound that inhibits MET, SRC, and CSF1R. comprising diagnosing the patient with a cancer mediated by a genetically altered MET. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



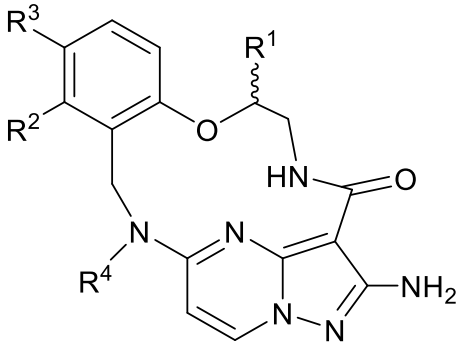
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or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



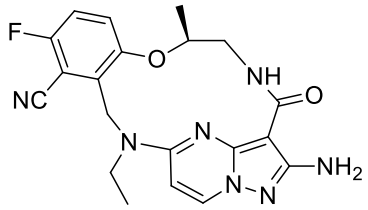
or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

**[014]** In another example~~aspect~~, the present disclosure provides a use of compound that inhibits MET, SRC, and CSF1R in the preparation of a medicament for the treatment of a disease in a patient. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



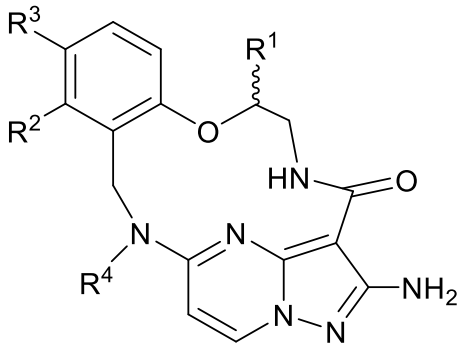
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or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



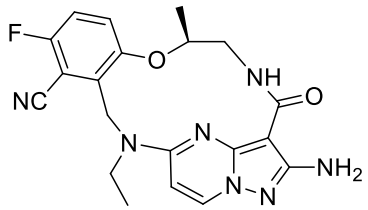
or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

**[015]** In another example~~aspect~~, the present disclosure provides a compound inhibits MET, SRC, and CSF1R for treating cancer in a patient. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



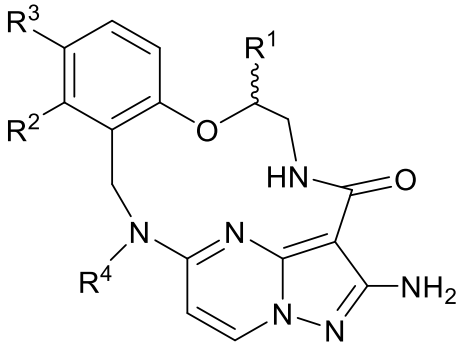
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or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



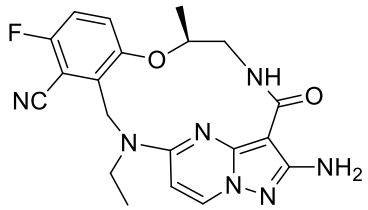
or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

**[016]** In another example~~aspect~~, the present disclosure provides use of a compound that inhibits MET, SRC, and CSF1R for treating cancer in a patient previously shown to express a genetically altered tyrosine or serine/threonine kinase. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



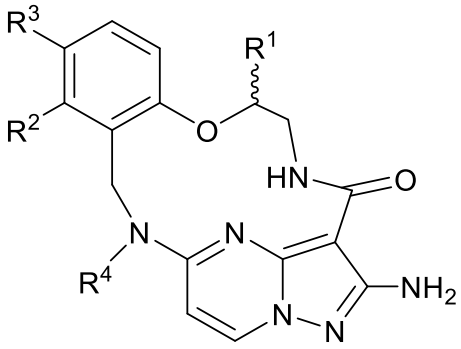
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or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

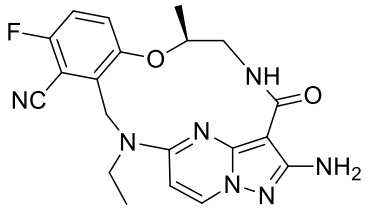
**[017]** In another example~~aspect~~, the present disclosure provide a use a compound inhibits MET, SRC, and CSF1R for treating cancer in a patient, wherein the patient has been previously treated with a cancer therapeutic, and the cancer has developed resistance to the cancer therapeutic. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



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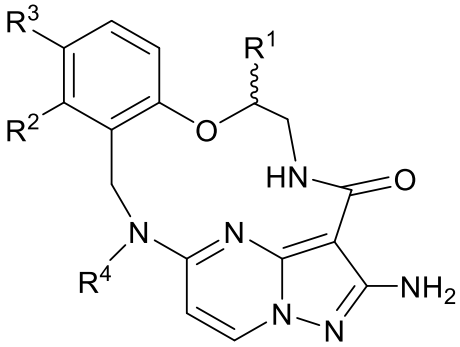
or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein.

In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

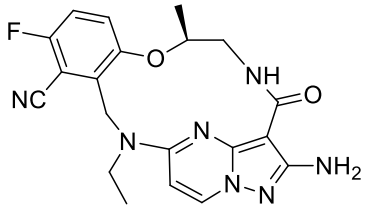
**[018]** In another example~~aspect~~, the present disclosure provides the use of a compound that inhibits MET, SRC, and CSF1R for treating cancer in a patient previously shown to express a genetically altered tyrosine or serine/threonine kinase, wherein the patient has been previously treated with a cancer therapeutic, and the cancer has developed resistance to the cancer therapeutic. In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula I



I

or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$, $R^3$, and $R^4$ are defined as described herein.

In some ~~embodiments~~examples, the compound that inhibits MET, SRC, and CSF1R is of the formula



or a pharmaceutically acceptable salt thereof. In some ~~embodiments~~examples, the patient, has received prior treatment with one or more therapeutic agents.

**[019]** In some ~~embodiments~~examples, the genetically altered MET gene comprising a point mutation that is expressed in the c-Met protein. In some examples~~embodiments~~, the genetically altered MET comprises a point mutation expressed in the c-Met protein at one or more of positions P991, T992, D1010, V1092, H1094, G1163, T1173, H1094, N1100, Y1003, H1106, V1070, V1188, V1092, H1094, G1162, L1195, F1200, V1220, D1228, Y1230, D1231, Y1235, D1246, Y1248, M1250, and M1268. In some examples~~embodiments~~, the genetically altered MET comprises a point mutation expressed in the c-Met protein that is selected from the group consisting of P991S, T992I, D1010H, D1010Y, V1092I, H1094N, H1094R, H1094Y, N1100K, N1100S, Y1003C, Y1003F, Y1003H, H1106D, V1070A, V1092I, V1188I, T1173I, H1094Y, G1163R, L1195F, F1195I, L1195V, F1200I, V1220I, D1228N, D1228H, D1228V, Y1230A, Y1230C, Y1230D, Y1230H, Y1230H, Y1230S, D1231Y, Y1235D, D1246N, D1246H, Y1248D, Y1248H, Y1248C, M1250T, and M1268T. In some examples~~embodiments~~, the genetically altered MET comprises a point mutation expressed in the c-Met protein that is selected from the group consisting of T1173I, P991S, M1250T, T992I, V1092I, F1200I, Y1235D, Y1230H, D1246N, D1246H, Y1248D, Y1248H, Y1248C, and M1268T. In some examples~~embodiments~~, the cancer is exhibiting bypass resistance. In some examples~~embodiments~~, the bypass resistance is mediated by a SRC/CSF1R.

**[020]** In some examples~~embodiments~~, the cancer is a carcinoma, a sarcoma, a lymphoma, Hodgekin's disease, a melanoma, a mesothelioma, Burkitt's lymphoma, a nasopharyngeal carcinoma, a leukemia, a lung cancer, a breast cancer, a hereditary human papillary renal carcinoma, a sporadic human papillary renal carcinoma, a childhood hepatocellular carcinoma, or a myeloma. In some examples~~embodiments~~, the cancer is selected from the group consisting of ALCL, NSCLC, neuroblastoma, inflammatory myofibroblastic tumor, renal cancer, adult renal cell carcinoma, pediatric renal cell carcinoma, breast cancer, triple negative breast cancer, triple positive breast cancer, $HER^+$ breast cancer, mouth cancer, esophageal cancer, laryngeal cancer, pancreatic cancer, bladder cancer, colon cancer, colonic adenocarcinoma, glioblastoma, glioblastoma multiforme, thyroid cancer, anaplastic thyroid cancer, endocrine cancer, bone cancer, cholangiocarcinoma, ovarian cancer, cervical cancer, uterine cancer, testicular cancer, gastric cancer, gastric adenocarcinoma, colorectal cancer, rectal cancer, liver cancer, kidney cancer, angiosarcoma, epithelioid hemangioendothelioma, intrahepatic cholangiocarcinoma, thyroid papillary cancer, spitzoid neoplasms, sarcoma, astrocytoma, brain lower grade glioma, secretory breast carcinoma, mammary analogue carcinoma, acute myeloid leukemia, congenital mesoblastic nephroma, congenital

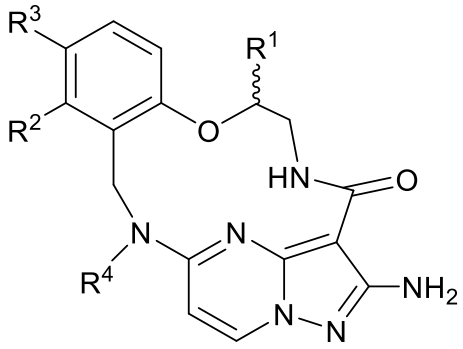
fibrosarcomas, Ph-like acute lymphoblastic leukemia, thyroid carcinoma, skin cancer, head and neck squamous cell carcinoma, pediatric glioma CML, prostate cancer, lung squamous carcinoma, ovarian serous cystadenocarcinoma, skin cutaneous melanoma, metastatic castration-resistant prostate cancer, Hodgkin lymphoma, neuroendocrine tumors, serous and clear cell endometrial cancer.

**[021]** In some examples~~embodiments~~, the patient has been previously treated with a cancer therapeutic. In some examples~~embodiments~~, the patient has been previously treated with a cancer therapeutic, and the cancer has developed resistance to the cancer therapeutic. In some examples~~embodiments~~, the resistance is a primary intrinsic resistance. In some examples~~embodiments~~, the resistance is an acquired resistance from mutation(s). In some examples~~embodiments~~, the resistance is a bypass resistance. In some examples~~embodiments~~, the resistance is an EMT-based resistance.

**[022]** Additional examples~~embodiments~~, features, and advantages of the disclosure will be apparent from the following detailed description and through practice of the disclosure. The compounds of the present disclosure can be described as examples~~embodiments~~ in any of the following enumerated clauses. It will be understood that any of the examples~~embodiments~~ described herein can be used in connection with any other examples~~embodiments~~ described herein to the extent that the examples~~embodiments~~ do not contradict one another.

**[023]** 1. A method of treating cancer in a patient comprising, administering to the patient a therapeutically effective amount of a compound that inhibits MET, SRC and CSF1R, wherein the cancer is mediated by a genetically altered MET.

**[024]** 2. The method of clause 1, wherein the compound of the formula



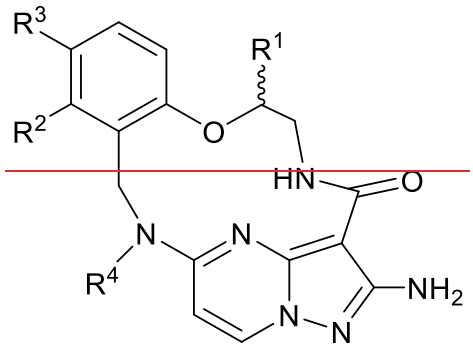

wherein

$R^1$ is H, deuterium, or $C_1$-$C_6$ alkyl;

$R^2$ is chloro or -CN;

WHAT IS CLAIMED IS:

1. A method of treating cancer in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound that inhibits MET, SRC and CSF1R, wherein the cancer is mediated by a genetically altered MET, wherein the compound is of formula



wherein

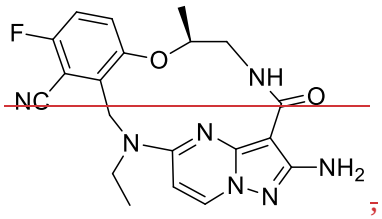
$R^1$ is H, deuterium, or $C_1$-$C_6$ alkyl;

$R^2$ is chloro or -CN;

$R^3$ is H, deuterium, or fluoro;

$R^4$ is H or $C_1$-$C_6$ alkyl, wherein each hydrogen atom in $C_1$-$C_6$ alkyl is independently optionally substituted by deuterium, fluoro, chloro, bromo, -OH, -CN, -O$C_1$-$C_6$ alkyl, -$NH_2$, -NH($C_1$-$C_6$ alkyl), -N($C_1$-$C_6$ alkyl)$_2$, or $C_3$-$C_7$ cycloalkyl, or a pharmaceutically acceptable salt thereof.

2. The method of claim 1, wherein the compound is of the formula



;

or a pharmaceutically acceptable salt thereof.

3. The method of claim 1 or 2, wherein the cancer is a carcinoma, a sarcoma, a lymphoma, Hodgekin's disease, a melanoma, a mesothelioma, Burkitt's lymphoma, a nasopharyngeal carcinoma, a leukemia, a lung cancer, a breast cancer, a hereditary human papillary renal carcinoma, a sporadic human papillary renal carcinoma, a childhood hepatocellular carcinoma, or a myeloma.

~~4. The method of any one of claims 1 to 3, wherein the cancer is selected from the group consisting of ALCL, NSCLC, neuroblastoma, inflammatory myofibroblastic tumor, renal cancer, adult renal cell carcinoma, pediatric renal cell carcinoma, breast cancer, triple negative breast cancer, triple positive breast cancer, $HER^+$ breast cancer, mouth cancer, esophageal cancer, laryngeal cancer, pancreatic cancer, bladder cancer, colon cancer, colonic adenocarcinoma, glioblastoma, glioblastoma multiforme, thyroid cancer, anaplastic thyroid cancer, endocrine cancer, bone cancer, cholangiocarcinoma, ovarian cancer, cervical cancer, uterine cancer, testicular cancer, gastric cancer, gastric adenocarcinoma, colorectal cancer, rectal cancer, liver cancer, kidney cancer, angiosarcoma, epithelioid hemangioendothelioma, intrahepatic cholangiocarcinoma, thyroid papillary cancer, spitzoid neoplasms, sarcoma, astrocytoma, brain lower grade glioma, secretory breast carcinoma, mammary analogue carcinoma, acute myeloid leukemia, congenital mesoblastic nephroma, congenital fibrosarcomas, Ph-like acute lymphoblastic leukemia, thyroid carcinoma, skin cancer, head and neck squamous cell carcinoma, pediatric glioma CML, prostate cancer, lung squamous carcinoma, ovarian serous cystadenocarcinoma, skin cutaneous melanoma, metastatic castration-resistant prostate cancer, Hodgkin lymphoma, neuroendocrine tumors, and serous and clear cell endometrial cancer.~~

~~5. The method of any one of the preceding claims, wherein the patient has received prior treatment with one or more therapeutic agents.~~

~~6. The method of any one of the preceding claims, wherein the cancer is mediated by a genetically altered MET.~~

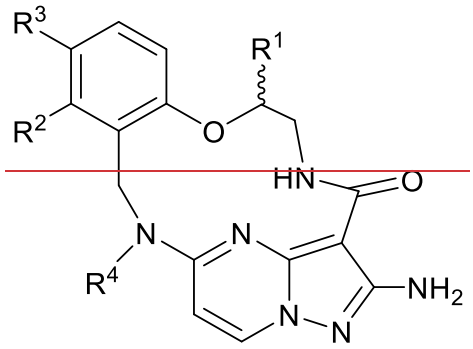
~~7. The method of claim 5, wherein the genetically altered MET encodes a point mutation that is expressed in the c-Met protein.~~

~~8. The method of any one of claims 6 to 7, wherein the genetically altered MET encodes a point mutation expressed in the c-Met protein at one or more of positions P991, T992, V1092, H1094, G1163, T1173, L1195, F1200, D1228, Y1230, Y1235, D1246, Y1248, M1250, and M1268.~~

9. The method of any one of claims 6 to 8, wherein the genetically altered MET encodes a point mutation expressed in the c-Met protein that is selected from the group consisting of T1173I, P991S, M1250T, T992I, V1092I, F1200I, Y1235D, Y1230H, D1246N, D1246H, Y1248D, Y1248H, Y1248C, and M1268T.

10. The method of any one of claims 6 to 9, wherein the cancer is exhibiting bypass resistance mediated by a SRC/CSF1R.

11. A compound that inhibits MET, SRC and CSF1R for use in treating cancer in a patient, wherein the cancer is mediated by a genetically altered MET, the compound having formula




wherein

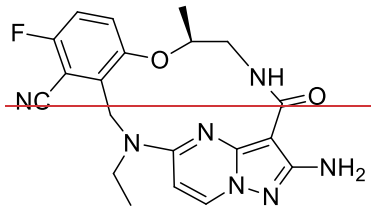
$R^1$ is H, deuterium, or $C_1$-$C_6$ alkyl;

$R^2$ is chloro or -CN;

$R^3$ is H, deuterium, or fluoro;

$R^4$ is H or $C_1$-$C_6$ alkyl, wherein each hydrogen atom in $C_1$-$C_6$ alkyl is independently optionally substituted by deuterium, fluoro, chloro, bromo, -OH, -CN, -$OC_1$-$C_6$ alkyl, -$NH_2$, -NH($C_1$-$C_6$ alkyl), -N($C_1$-$C_6$ alkyl)$_2$, or $C_3$-$C_7$ cycloalkyl, or a pharmaceutically acceptable salt thereof.

12. The compound of claim 11, wherein the compound is of formula



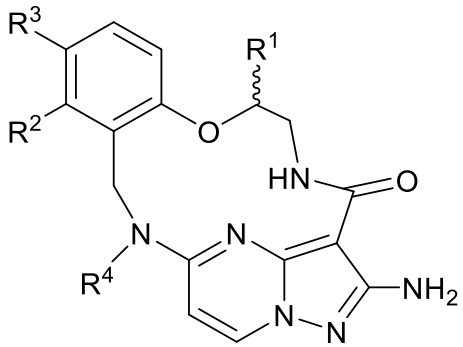

or a pharmaceutically acceptable salt thereof.

~~13. The compound for use of claim 11 or 12, wherein the cancer is a carcinoma, a sarcoma, a lymphoma, Hodgekin's disease, a melanoma, a mesothelioma, Burkitt's lymphoma, a nasopharyngeal carcinoma, a leukemia, a lung cancer, a breast cancer, a hereditary human papillary renal carcinoma, a sporadic human papillary renal carcinoma, a childhood hepatocellular carcinoma, or a myeloma.~~

~~14. The compound for use of claim 11 or 12, wherein the cancer is selected from the group consisting of ALCL, NSCLC, neuroblastoma, inflammatory myofibroblastic tumor, renal cancer, adult renal cell carcinoma, pediatric renal cell carcinoma, breast cancer, triple negative breast cancer, triple positive breast cancer, $HER^+$ breast cancer, mouth cancer, esophageal cancer, laryngeal cancer, pancreatic cancer, bladder cancer, colon cancer, colonic adenocarcinoma, glioblastoma, glioblastoma multiforme, thyroid cancer, anaplastic thyroid cancer, endocrine cancer, bone cancer, cholangiocarcinoma, ovarian cancer, cervical cancer, uterine cancer, testicular cancer, gastric cancer, gastric adenocarcinoma, colorectal cancer, rectal cancer, liver cancer, kidney cancer, angiosarcoma, epithelioid hemangioendothelioma, intrahepatic cholangiocarcinoma, thyroid papillary cancer, spitzoid neoplasms, sarcoma, astrocytoma, brain lower grade glioma, secretory breast carcinoma, mammary analogue carcinoma, acute myeloid leukemia, congenital mesoblastic nephroma, congenital fibrosarcomas, Ph-like acute lymphoblastic leukemia, thyroid carcinoma, skin cancer, head and neck squamous cell carcinoma, pediatric glioma CML, prostate cancer, lung squamous carcinoma, ovarian serous cystadenocarcinoma, skin cutaneous melanoma, metastatic castration-resistant prostate cancer, Hodgkin lymphoma, neuroendocrine tumors, and serous and clear cell endometrial cancer.~~

~~15. The compound of any one of claims 11 to 14, wherein the patient has received prior treatment with one or more therapeutic agents.~~

~~16~~1. Use of a compound ~~that inhibits MET, SRC and CSF1R~~ in the preparation of a medicament for treating cancer in a patient, ~~wherein the cancer is mediated by a genetically altered MET, and~~ wherein the compound is of formula



wherein

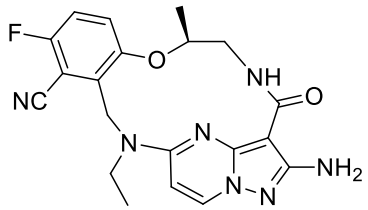
$R^1$ is H, deuterium, or $C_1$-$C_6$ alkyl;

$R^2$ is chloro or -CN;

$R^3$ is H, deuterium, or fluoro;

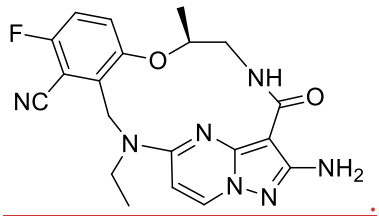
$R^4$ is H or $C_1$-$C_6$ alkyl, wherein each hydrogen atom in $C_1$-$C_6$ alkyl is independently optionally substituted by deuterium, fluoro, chloro, bromo, -OH, -CN, -O$C_1$-$C_6$ alkyl, -$NH_2$, -NH($C_1$-$C_6$ alkyl), -N($C_1$-$C_6$ alkyl)$_2$, or $C_3$-$C_7$ cycloalkyl, or a pharmaceutically acceptable salt thereof.

~~17~~2. The use of claim ~~16~~1, wherein the compound is of formula



or a pharmaceutically acceptable salt thereof.

3. The use of claim 1, wherein the compound is of formula



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~~18~~4. The use of ~~claim 16 or 17~~any one of claims 1 to 3, wherein the cancer is a carcinoma, a sarcoma, a lymphoma, Hodgekin's disease, a melanoma, a mesothelioma, Burkitt's lymphoma, a nasopharyngeal carcinoma, a leukemia, a lung cancer, a breast cancer, a hereditary human papillary

renal carcinoma, a sporadic human papillary renal carcinoma, a childhood hepatocellular carcinoma, or a myeloma.

~~19~~5. The use of ~~claim 16 or 17~~any one of claims 1 to 3, wherein the cancer is selected from the group consisting of ALCL, NSCLC, neuroblastoma, inflammatory myofibroblastic tumor, renal cancer, adult renal cell carcinoma, pediatric renal cell carcinoma, breast cancer, triple negative breast cancer, triple positive breast cancer, $HER^+$ breast cancer, mouth cancer, esophageal cancer, laryngeal cancer, pancreatic cancer, bladder cancer, colon cancer, colonic adenocarcinoma, glioblastoma, glioblastoma multiforme, thyroid cancer, anaplastic thyroid cancer, endocrine cancer, bone cancer, cholangiocarcinoma, ovarian cancer, cervical cancer, uterine cancer, testicular cancer, gastric cancer, gastric adenocarcinoma, colorectal cancer, rectal cancer, liver cancer, kidney cancer, angiosarcoma, epithelioid hemangioendothelioma, intrahepatic cholangiocarcinoma, thyroid papillary cancer, spitzoid neoplasms, sarcoma, astrocytoma, brain lower grade glioma, secretory breast carcinoma, mammary analogue carcinoma, acute myeloid leukemia, congenital mesoblastic nephroma, congenital fibrosarcomas, Ph-like acute lymphoblastic leukemia, thyroid carcinoma, skin cancer, head and neck squamous cell carcinoma, pediatric glioma CML, prostate cancer, lung squamous carcinoma, ovarian serous cystadenocarcinoma, skin cutaneous melanoma, metastatic castration-resistant prostate cancer, Hodgkin lymphoma, neuroendocrine tumors, and serous and clear cell endometrial cancer.

~~20~~6. The use of any one of claims ~~16~~ 1 to ~~19~~5, wherein the patient has received prior treatment with one or more therapeutic agents.

7. The use of any one of claims 1 to 6, wherein the cancer is mediated by a genetically altered MET.

8. The use of claim 7, wherein the genetically altered MET encodes a point mutation that is expressed in the c-Met protein.

9. The use of any one of claims 7 to 8, wherein the genetically altered MET encodes a point mutation expressed in the c-Met protein at one or more of positions P991, T992, V1092, H1094, G1163, T1173, L1195, F1200, D1228, Y1230, Y1235, D1246, Y1248, M1250, and M1268.

10. The use of any one of claims 7 to 9, wherein the genetically altered MET encodes a point mutation expressed in the c-Met protein that is selected from the group consisting of T1173I, P991S, M1250T, T992I, V1092I, F1200I, Y1235D, Y1230H, D1246N, D1246H, Y1248D, Y1248H, Y1248C, and M1268T.

11. The use of any one of claims 7 to 10, wherein the cancer is exhibiting bypass resistance mediated by a SRC/CSF1R.