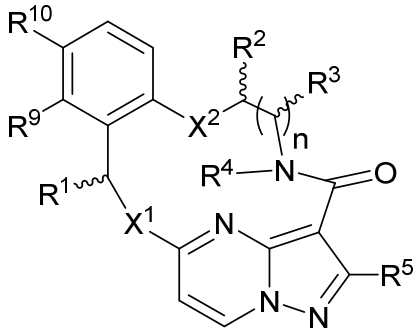
often detected in invasive tumors. Autocrine CSF-1R activation induced hyperproliferation and disruption of junctional integrity in acinar structures formed by human mammary epithelial cells in three-dimensional culture through a SRC-dependent mechanism (Wrobel CN, et al. Autocrine CSF1R activation promotes SRC-dependent disruption of mammary epithelial architecture. *J Cell Biol.* **2004**, 165, 263-273). Inhibition of CSF-1R and SRC may prove to be a valuable strategy in the treatment of invasive tumors. Tenosynovial giant cell tumor (TGCT) or pigmented villonodular synovitis (PVNS) is a clonal neoplastic proliferation arising from cells overexpressing CSF1 that recruit CSF1R-bearing polyclony macrophages and make up the bulk of the tumor. Inhibition of CSF1R using small molecule inhibitors can lead to improvement in the affected joint (Ravi V, et al. Treatment of tenosynovial giant cell tumor and pigmented villonodular synovitis. *Curr Opin Oncol*. **2011**, 23, 361-366).

[010] In a summary, aberrant activation of HGF/MET pathway has frequently been found in human cancers *via* protein over-expression, mutation, gene amplification, and also paracrine or autocrine upregulation. In addition, the activation of HGF/MET signaling confers resistance to cancer therapies. SRC activation is implicated for ligand-dependent and independent activation of MET. CSF1R plays an import role in regulation of tumor associated macrophage. Therefore, the polypharmacologic inhibition of MET/SRC/CSF1R has great potential for therapeutic interventions in cancers. To-date, compounds that inhibit MET/SRC and/or CSF1R have been elusive. As such, there exists a significant unmet need.

SUMMARY

[011] The disclosure relates to a compound of the Formula I



I

[012] or a pharmaceutically acceptable salt thereof, wherein

[013] X^1 and X^2 are independently $–CR^6R^7$-, S, S(O), $S(O)_2$, O or $N(R^8)$;

[014] R^1 is H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_{10} aryl, $-C(O)OR^8$ or $-C(O)NR^8R^9$; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_6-C_{10} aryl is independently optionally

[016] R^4 is H, C_1-C_6 alkyl or 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C_1-C_6 alkyl or 3-to 7-membered heterocycloalkyl is independently optionally substituted by halogen, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

[017] R^5 is H or -NR^6R^7;

[018] each R^6, R^7 and R^8 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and C_3-C_6 cycloalkyl; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and C_3-C_6 cycloalkyl 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)$_2$, C_3-C_7 cycloalkyl, 3-to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 7-membered heteroaryl, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), or -C(O)N(C_1-C_6 alkyl)$_2$;

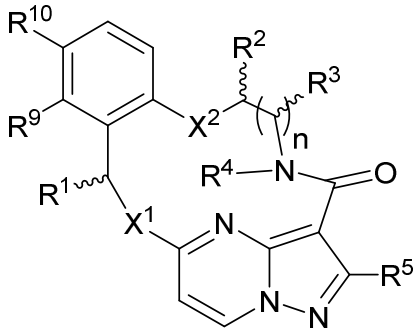
[019] R^9 is H, fluoro, chloro, bromo, -CN, -CF_3, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl) and -C(O)N(C_1-C_6 alkyl)$_2$;

[020] R^{10} is H, fluoro, chloro or bromo; and

[021] n is 1 or 2;

[022] with the proviso that when R^5 is H, R^9 is selected from the group consisting of -CN, -CF_3, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl) and -C(O)N(C_1-C_6 alkyl)$_2$.

[0022a] In an aspect, there is provided a compound of the Formula I



I

or a pharmaceutically acceptable salt thereof, wherein

X^1 and X^2 are independently -CR^6R^7-, S, S(O), S(O)$_2$, O or N(R^8);

R^1 is H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_{10} aryl, -C(O)OR^8 or -C(O)NR^8R^9; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_6-C_{10} aryl is independently optionally

substituted by deuterium, halogen, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)C_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)C_1-C_6 alkyl, -NHC(O)NH_2, -NHC(O)NHC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NHC_1-C_6 alkyl, -NHC(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)$_2$, -NHC(O)OC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)OC_1-C_6 alkyl, -NHS(O)(C_1-C_6 alkyl), -NHS(O)$_2$(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$(C_1-C_6 alkyl), -NHS(O)NH_2, -NHS(O)$_2NH_2$, -N(C_1-C_6 alkyl)S(O)NH_2, -N(C_1-C_6 alkyl)S(O)$_2NH_2$, -NHS(O)NH(C_1-C_6 alkyl), -NHS(O)$_2$NH(C_1-C_6 alkyl), -NHS(O)N(C_1-C_6 alkyl)$_2$, -NHS(O)$_2$N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)$_2$N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, -SC_1-C_6 alkyl, -S(O)C_1-C_6 alkyl, -S(O)$_2C_1$-C_6 alkyl, -S(O)NH(C_1-C_6 alkyl), -S(O)$_2$NH(C_1-C_6 alkyl), -S(O)N(C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_1-C_6 alkyl)$_2$, -P(C_1-C_6 alkyl)$_2$, -P(O)(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or 3- to 7-membered heterocycloalkyl;

each R^2 and R^3 is independently H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{10} aryl, -C(O)OR^8 or -C(O)NR^8R^9; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_6-C_{10} aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)C_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)C_1-C_6 alkyl, -NHC(O)NH_2, -NHC(O)NHC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NHC_1-C_6 alkyl, -NHC(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)$_2$, -NHC(O)OC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)OC_1-C_6 alkyl, -NHS(O)(C_1-C_6 alkyl), -NHS(O)$_2$(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$(C_1-C_6 alkyl), -NHS(O)NH_2, -NHS(O)$_2NH_2$, -N(C_1-C_6 alkyl)S(O)NH_2, -N(C_1-C_6 alkyl)S(O)$_2NH_2$, -NHS(O)NH(C_1-C_6 alkyl), -NHS(O)$_2$NH(C_1-C_6 alkyl), -NHS(O)N(C_1-C_6 alkyl)$_2$, -NHS(O)$_2$N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)$_2$N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, -SC_1-C_6 alkyl, -S(O)C_1-C_6 alkyl, -S(O)$_2C_1$-C_6 alkyl, -S(O)NH(C_1-C_6 alkyl), -S(O)$_2$NH(C_1-C_6 alkyl), -S(O)N(C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_1-C_6 alkyl)$_2$, -P(C_1-C_6 alkyl)$_2$, -P(O)(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or 3- to 7-membered heterocycloalkyl; or R^2 and R^3 taken together with the carbon atoms to which they are attached optionally form a C_5-C_7 cycloalkyl or a 5- to 7-membered heterocycloalkyl; or R^2 and R^4 taken together with the atoms to which they are attached optionally form a 5- to 7-membered heterocycloalkyl;

R^4 is H, C_1-C_6 alkyl or 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C_1-C_6 alkyl or 3-to 7-membered heterocycloalkyl is independently optionally substituted by halogen, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

R^5 is -NR^6R^7;

each R^6, R^7 and R^8 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and C_3-C_6 cycloalkyl; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and C_3-C_6 cycloalkyl 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)$_2$, C_3-C_7 cycloalkyl, 3-to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 7-membered heteroaryl, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), or -C(O)N(C_1-C_6 alkyl)$_2$;

R^9 is H, fluoro, chloro, bromo, -CN, -CF_3, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl) and -C(O)N(C_1-C_6 alkyl)$_2$;

R^{10} is H, fluoro, chloro or bromo; and

n is 1 or 2.

[022b] In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent, carrier or excipient.

[023] The disclosure relates to a pharmaceutical composition comprising a compound of the Formula I, or a pharmaceutically acceptable salt thereof, and optionally at least one or more of a pharmaceutically acceptable diluent, carrier or excipient.

[024] The disclosure is directed to a method of treating cancer in a patient comprising,

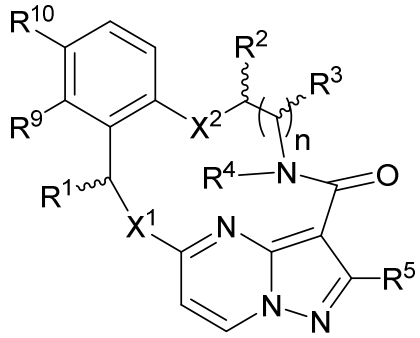
[025] a. administering a therapeutically effective amount of a compound that inhibits SRC and MET, and/or CSF1R. In some examples, the compound that inhibits SRC and MET, and/or CSF1R is of the Formula I. In someexamples, the cancer is gastric cancer, colon cancer, renal cancer, liver cancer, lung cancer, glioblastoma, or head & neck cancer.

[026] The disclosure is directed to a method of treating cancer in a patient comprising,

[027] a. administering a therapeutically effective amount of a compound that inhibits SRC and MET, and/or CSF1R; and

WHAT IS CLAIMED IS:

1. A compound of the Formula I



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or a pharmaceutically acceptable salt thereof, wherein

X^1 and X^2 are independently $-CR^6R^7-$, S, S(O), $S(O)_2$, O or $N(R^8)$;

R^1 is H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_{10} aryl, $-C(O)OR^8$ or $-C(O)NR^8R^9$; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_6-C_{10} aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, $-OC_1$-C_6 alkyl, $-NH_2$, $-NH(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl$)_2$, $-NHC(O)C_1$-C_6 alkyl, $-N(C_1$-C_6 alkyl$)C(O)C_1$-C_6 alkyl, $-NHC(O)NH_2$, $-NHC(O)NHC_1$-C_6 alkyl, $-N(C_1$-C_6 alkyl$)C(O)NH_2$, $-N(C_1$-C_6 alkyl$)C(O)NHC_1$-C_6 alkyl, $-NHC(O)N(C_1$-C_6 alkyl$)_2$, $-N(C_1$-C_6 alkyl$)C(O)N(C_1$-C_6 alkyl$)_2$, $-NHC(O)OC_1$-C_6 alkyl, $-N(C_1$-C_6 alkyl$)C(O)OC_1$-C_6 alkyl, $-NHS(O)(C_1$-C_6 alkyl), $-NHS(O)_2(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl$)S(O)(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl$)S(O)_2(C_1$-C_6 alkyl), $-NHS(O)NH_2$, $-NHS(O)_2NH_2$, $-N(C_1$-C_6 alkyl$)S(O)NH_2$, $-N(C_1$-C_6 alkyl$)S(O)_2NH_2$, $-NHS(O)NH(C_1$-C_6 alkyl), $-NHS(O)_2NH(C_1$-C_6 alkyl), $-NHS(O)N(C_1$-C_6 alkyl$)_2$, $-NHS(O)_2N(C_1$-C_6 alkyl$)_2$, $-N(C_1$-C_6 alkyl$)S(O)NH(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl$)S(O)_2NH(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl$)S(O)N(C_1$-C_6 alkyl$)_2$, $-N(C_1$-C_6 alkyl$)S(O)_2N(C_1$-C_6 alkyl$)_2$, $-CO_2H$, $-C(O)OC_1$-C_6 alkyl, $-C(O)NH_2$, $-C(O)NH(C_1$-C_6 alkyl), $-C(O)N(C_1$-C_6 alkyl$)_2$, $-SC_1$-C_6 alkyl, $-S(O)C_1$-C_6 alkyl, $-S(O)_2C_1$-C_6 alkyl, $-S(O)NH(C_1$-C_6 alkyl), $-S(O)_2NH(C_1$-C_6 alkyl), $-S(O)N(C_1$-C_6 alkyl$)_2$, $-S(O)_2N(C_1$-C_6 alkyl$)_2$, $-P(C_1$-C_6 alkyl$)_2$, $-P(O)(C_1$-C_6 alkyl$)_2$, C_3-C_6 cycloalkyl, or 3- to 7-membered heterocycloalkyl;

each R^2 and R^3 is independently H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{10} aryl, $-C(O)OR^8$ or $-C(O)NR^8R^9$; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_6-C_{10} aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, $-OC_1$-C_6 alkyl, $-NH_2$,

-NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)C_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)C_1-C_6 alkyl, -NHC(O)NH_2, -NHC(O)NHC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NHC_1-C_6 alkyl, -NHC(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)$_2$, -NHC(O)OC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)OC_1-C_6 alkyl, -NHS(O)(C_1-C_6 alkyl), -NHS(O)$_2$(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$(C_1-C_6 alkyl), -NHS(O)NH_2, -NHS(O)$_2NH_2$, -N(C_1-C_6 alkyl)S(O)NH_2, -N(C_1-C_6 alkyl)S(O)$_2NH_2$, -NHS(O)NH(C_1-C_6 alkyl), -NHS(O)$_2$NH(C_1-C_6 alkyl), -NHS(O)N(C_1-C_6 alkyl)$_2$, -NHS(O)$_2$N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)$_2$N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, -SC_1-C_6 alkyl, -S(O)C_1-C_6 alkyl, -S(O)$_2C_1$-C_6 alkyl, -S(O)NH(C_1-C_6 alkyl), -S(O)$_2$NH(C_1-C_6 alkyl), -S(O)N(C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_1-C_6 alkyl)$_2$, -P(C_1-C_6 alkyl)$_2$, -P(O)(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or 3- to 7-membered heterocycloalkyl; or R^2 and R^3 taken together with the carbon atoms to which they are attached optionally form a C_5-C_7 cycloalkyl or a 5- to 7-membered heterocycloalkyl; or R^2 and R^4 taken together with the atoms to which they are attached optionally form a 5- to 7-membered heterocycloalkyl;

R^4 is H, C_1-C_6 alkyl or 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C_1-C_6 alkyl or 3-to 7-membered heterocycloalkyl is independently optionally substituted by halogen, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

R^5 is -NR^6R^7;

each R^6, R^7 and R^8 are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and C_3-C_6 cycloalkyl; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and C_3-C_6 cycloalkyl 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)$_2$, C_3-C_7 cycloalkyl, 3-to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 7-membered heteroaryl, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), or -C(O)N(C_1-C_6 alkyl)$_2$;

R^9 is H, fluoro, chloro, bromo, -CN, -CF_3, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl) and -C(O)N(C_1-C_6 alkyl)$_2$;

R^{10} is H, fluoro, chloro or bromo; and

n is 1 or 2.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^9 is -CN.

3. The compound of claim 2, or a pharmaceutically acceptable salt thereof, wherein R^{10} is F.

4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^6 and R^7 are H.

5. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein R^9 is -CN.

6. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein R^{10} is fluoro.

7. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X^1 is $N(R^8)$.

8. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^8 is C_1-C_6 alkyl, wherein each hydrogen atom is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, C_3-C_7 cycloalkyl, 3-to 7-membered heterocycloalkyl, C_6-C_{10} aryl, 5- to 7-membered heteroaryl, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), or -C(O)N(C_1-C_6 alkyl)$_2$.

9. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^8 is ethyl, propyl, iso-propyl, or methylcyclopropyl.

10. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein X^2 is O.

11. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^2 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{10} aryl, -C(O)OR^7 or -C(O)NR^7R^8; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_6-C_{10} aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl),

-N(C_1-C_6 alkyl)$_2$, -NHC(O)C_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)C_1-C_6 alkyl, -NHC(O)NH_2, -NHC(O)NHC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NHC_1-C_6 alkyl, -NHC(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)$_2$, -NHC(O)OC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)OC_1-C_6 alkyl, -NHS(O)(C_1-C_6 alkyl), -NHS(O)$_2$(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$(C_1-C_6 alkyl), -NHS(O)NH_2, -NHS(O)$_2NH_2$, -N(C_1-C_6 alkyl)S(O)NH_2, -N(C_1-C_6 alkyl)S(O)$_2NH_2$, -NHS(O)NH(C_1-C_6 alkyl), -NHS(O)$_2$NH(C_1-C_6 alkyl), -NHS(O)N(C_1-C_6 alkyl)$_2$, -NHS(O)$_2$N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)$_2$N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, -SC_1-C_6 alkyl, -S(O)C_1-C_6 alkyl, -S(O)$_2C_1$-C_6 alkyl, -S(O)NH(C_1-C_6 alkyl), -S(O)$_2$NH(C_1-C_6 alkyl), -S(O)N(C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_1-C_6 alkyl)$_2$, -P(C_1-C_6 alkyl)$_2$, -P(O)(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or 3-to 7-membered heterocycloalkyl, and R^3 is H.

12. The compound of claim 11, or a pharmaceutically acceptable salt thereof, wherein R^2 is C_1-C_6 alkyl.

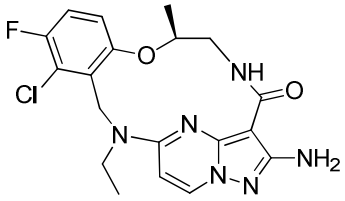
13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein R^2 is methyl.

14. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 is H, and R^3 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{10} aryl, -C(O)OR^7 or -C(O)NR^7R^8; wherein each hydrogen atom in C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_6-C_{10} aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC_1-C_6 alkyl, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)C_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)C_1-C_6 alkyl, -NHC(O)NH_2, -NHC(O)NHC_1-C_6 alkyl, N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NHC_1-C_6 alkyl, -NHC(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)$_2$, -NHC(O)OC_1-C_6 alkyl, -N(C_1-C_6 alkyl)C(O)OC_1-C_6 alkyl, -NHS(O)(C_1-C_6 alkyl), -NHS(O)$_2$(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$(C_1-C_6 alkyl), -NHS(O)NH_2, -NHS(O)$_2NH_2$, -N(C_1-C_6 alkyl)S(O)NH_2, -N(C_1-C_6 alkyl)S(O)$_2NH_2$, -NHS(O)NH(C_1-C_6 alkyl), -NHS(O)$_2$NH(C_1-C_6 alkyl), -NHS(O)N(C_1-C_6 alkyl)$_2$, -NHS(O)$_2$N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)$_2$NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)S(O)N(C_1-C_6 alkyl)$_2$, -N(C_1-C_6 alkyl)S(O)$_2$N(C_1-C_6 alkyl)$_2$, -CO_2H, -C(O)OC_1-C_6 alkyl, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, -SC_1-C_6 alkyl,

-S(O)C_1-C_6 alkyl, -S(O)$_2$$C_1$-$C_6$ alkyl, -S(O)NH(C_1-C_6 alkyl), -S(O)$_2$NH(C_1-C_6 alkyl), -S(O)N(C_1-C_6 alkyl)$_2$, -S(O)$_2$N(C_1-C_6 alkyl)$_2$, -P(C_1-C_6 alkyl)$_2$, -P(O)(C_1-C_6 alkyl)$_2$, C_3-C_6 cycloalkyl, or 3-to 7-membered heterocycloalkyl.

15. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are H.

16. The compound of claim 1, selected from the group consisting of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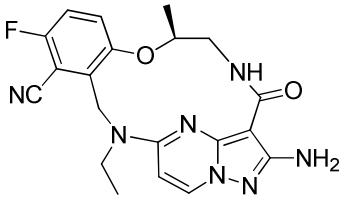
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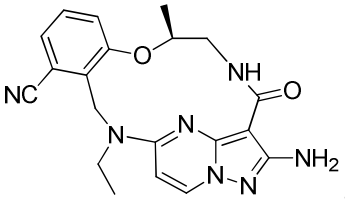
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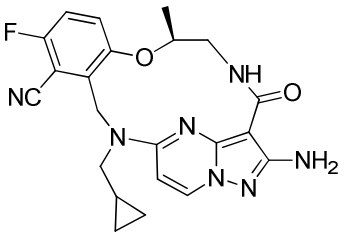
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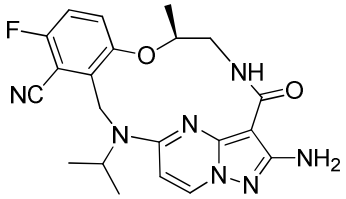
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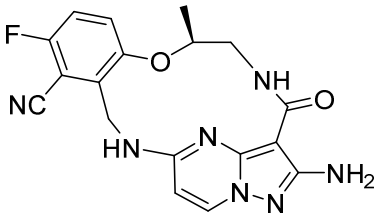
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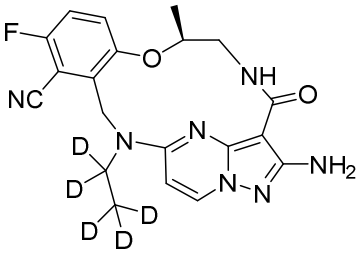
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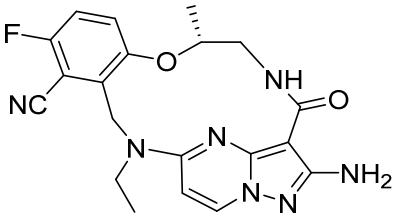
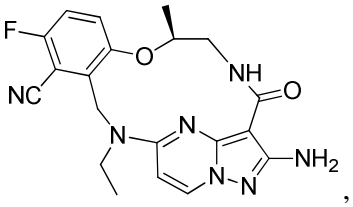


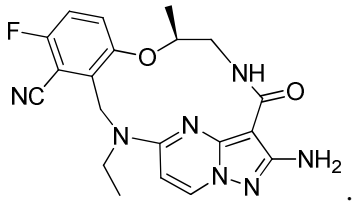
or a pharmaceutically acceptable salt thereof.

17. The compound of claim 1 having the structure:


,

or a pharmaceutically acceptable salt thereof.

18. The compound of claim 1 having the structure:



19. A pharmaceutical composition comprising a compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent, carrier or excipient.

20. A compound according to any one of claims 1 to 18 that inhibits SRC and MET, and/or CSF1R, or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer in a patient.

21. The compound for use of claim 20, wherein the cancer is gastric cancer, colon cancer, renal cancer, liver cancer, lung cancer, glioblastoma, or head & neck cancer.

22. The compound for use of claim 20 or 21, in combination with a therapeutically effective amount of at least one additional anti-cancer agent.

23. The compound for use of claim 22, wherein the at least one additional anti-cancer agent is an EGFR inhibitor, or a pharmaceutically acceptable salt thereof.

24. The compound for use of claim 22, wherein the additional anti-cancer agent is an antibody of EGFR.

25. The compound for use of claim 24, wherein the antibody of EGFR is cetuximab, necitumumab or panitumumab.

26. The compound for use of claim 22, wherein the additional anti-cancer agent is a small molecule inhibitor of EGFR.

27. The compound for use of claim 26, wherein the small molecule inhibitor of EGFR is afatinib, brigatinib, canertinib, dacomitinib, erlotinib, gefitinib, HKI 357, lapatinib, osimertinib,

naquotinib, nazartinib, neratinib, olmutinib, pelitinib, PF-06747775, rociletinib, vandetanib, or a pharmaceutically acceptable salt thereof.

28. Use of a compound according to any one of claims 1 to 18 that inhibits SRC and MET, and/or CSF1R, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer.

29. The use of claim 28, wherein the cancer is gastric cancer, colon cancer, renal cancer, liver cancer, lung cancer, glioblastoma, or head & neck cancer.

30. The use of claim 28 or 29, in combination with a therapeutically effective amount of at least one additional anti-cancer agent.

31. The use of claim 30, wherein the at least one additional anti-cancer agent is an EGFR inhibitor, or a pharmaceutically acceptable salt thereof.

32. The use of claim 30, wherein the additional anti-cancer agent is an antibody of EGFR.

33. The use of claim 32, wherein the antibody of EGFR cetuximab, necitumumab or panitumumab.

34. The use of claim 30, wherein the additional anti-cancer agent is a small molecule inhibitor of EGFR.

35. The use of claim 34, wherein the small molecule inhibitor of EGFR is afatinib, brigatinib, canertinib, dacomitinib, erlotinib, gefitinib, HKI 357, lapatinib, osimertinib, naquotinib, nazartinib, neratinib, olmutinib, pelitinib, PF-06747775, rociletinib, vandetanib, or a pharmaceutically acceptable salt thereof.