

INHIBITORS OF MET KINASE

CROSS-REFERENCE TO RELATED APPLICATION

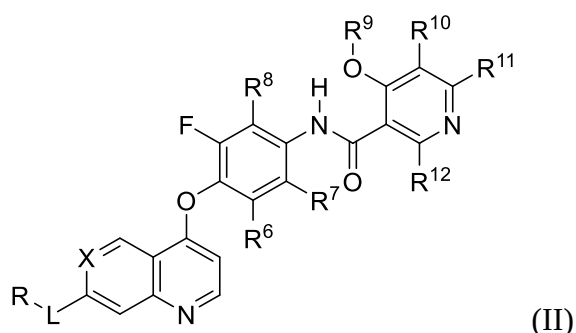
[0001] This application claims the benefit of U.S. Patent Application No. 63/290,291, filed on December 16, 2021; U.S. Patent Application No. 63/301,267, filed on January 20, 2022; U.S. Patent Application No. 63/380,049, filed on October 18, 2022; and U.S. Patent Application No. 63/386,647, filed on December 8, 2022; each of which is hereby incorporated by reference in its entirety.

BACKGROUND

[0002] MET is a member of the class IV receptor tyrosine kinase family and is expressed on the surfaces of many different cell types, including epithelial cells of many organs, including the liver, pancreas, prostate, kidney, muscle, and bone marrow, during both embryogenesis and adulthood. Binding of the hepatocyte growth factor induces dimerization and activation of the receptor. MET modulates many essential cellular processes during development and wound healing, including cell proliferation, survival, motility, and morphogenesis. Aberrant MET activity is found in many different human cancers. Accordingly, therapies that target MET kinase activity are desired for use in the treatment of cancer and other disorders characterized by aberrant MET pathway signaling.

BRIEF SUMMARY

[0002a] In an aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt or solvate thereof, having the structure of Formula (II):



wherein,

X is independently N, or C-L¹-R¹;

L is a bond, -O-, -NH-, -NHCO-, or -CONH-;

L¹ is a bond, -O-, -NH-, -NHCO-, or -CONH-;

R is selected from the group consisting of H, halogen, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkenyl, optionally substituted C1-C6 alkynyl, optionally

R¹ is selected from the group consisting of H, halogen, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkenyl, optionally substituted C1-C6 alkynyl, optionally substituted C3-C6 cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl, and optionally substituted heteroarylalkyl;

R⁹ is selected from the group consisting of optionally substituted C1-C6 alkyl, optionally substituted C3-C6 cycloalkyl, and optionally substituted cycloalkylalkyl;

R¹¹ is H, halogen, -NH₂, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkoxy, -NH(optionally substituted C1-C6 alkyl), or -N(optionally substituted C1-C6 alkyl)₂;

[0002b] In another aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt or solvate thereof, having the structure of Formula (III):



L¹ is a bond, -O-, -NH-, -NHCO-, or -CONH-;

1a

R¹ is selected from the group consisting of H, halogen, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkenyl, optionally substituted C1-C6 alkynyl, optionally substituted C3-C6 cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heteroaryl, and optionally substituted heteroarylalkyl;

R⁶, R⁷ and R⁸ are each independently selected from H or halogen; provided that at least one of R⁶, R⁷ or R⁸ is not H;

R⁹ is selected from the group consisting of optionally substituted C1-C6 alkyl, optionally substituted C3-C6 cycloalkyl, and optionally substituted cycloalkylalkyl;

R¹⁰ is H;

R¹¹ is H, halogen, -NH₂, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkoxy, -NH(optionally substituted C1-C6 alkyl), or -N(optionally substituted C1-C6 alkyl)₂;

R¹² is H, halogen, optionally substituted C1-C6 alkyl or optionally substituted C1-C6 alkoxy.

[0002c] In a further aspect of the present disclosure, there is provided a compound, or pharmaceutically acceptable salt or solvate thereof, selected from the group consisting of:

N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;

6-chloro-*N*-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide formate;

N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-ethoxypyridine-3-carboxamide;

N-(3-chloro-5-fluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinazolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinazolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;

N-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-2-fluoro-4-methoxypyridine-3-carboxamide;

N-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-ethoxypyridine-3-carboxamide;
N-(2,3-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxypyridine-3-carboxamide;
N-(2,3-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxypyridine-3-carboxamide;
N-(2,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
N-(4-((7-(3-(dimethylamino)propoxy)-6-methoxyquinolin-4-yl)oxy)-2,5-difluorophenyl)-4-ethoxypyridine-3-carboxamide;
N-[2,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-(2,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide;
6-chloro-*N*-[2,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-[2,5-difluoro-4-({6-methoxy-7-[3-(morpholin-4-yl)propoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxypyridine-3-carboxamide;
N-[3,5-difluoro-4-({6-methoxy-7-[2-(morpholin-4-yl)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
6-amino-*N*-(2,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
6-amino-*N*-[2,5-difluoro-4-({6-methoxy-7-[3-(morpholin-4-yl)propoxy]quinolin-4-yl}oxy)phenyl]-4-ethoxypyridine-3-carboxamide;

6-amino-*N*-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;

N-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(trifluoromethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-(4-((7-(difluoromethoxy)-6-methoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((7-(2-hydroxy-2-methylpropoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-(4-((6,7-bis(2-methoxyethoxy)quinolin-4-yl)oxy)-3,5-difluorophenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-6-fluoro-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxy-6-methylpyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxy-6-((2-methoxyethyl)amino)pyridine-3-carboxamide;

N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-(difluoromethoxy)pyridine-3-carboxamide;

N-(2,3-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(difluoromethoxy)pyridine-3-carboxamide;

4-methoxy-*N*-[2,3,5-trifluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]pyridine-3-carboxamide;

4-ethoxy-*N*-(2,3,5-trifluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

N-[2,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-propoxypyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

4-cyclopropoxy-*N*-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]pyridine-3-carboxamide;

4-cyclobutoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

N-[3,5-difluoro-4-((6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl)oxy)phenyl]-4-propoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(3,3-difluorocyclobutoxy)pyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(3-fluoropropoxy)pyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-isopropoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)pyridine-3-carboxamide;
(R)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-fluoropropoxy)pyridine-3-carboxamide;
(S)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-fluoropropoxy)pyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxyethoxy)pyridine-3-carboxamide;
(S)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxypropoxy)pyridine-3-carboxamide;
(R)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxypropoxy)pyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxy-2-methylpropoxy)pyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-methoxyethoxy)pyridine-3-carboxamide;
4-butoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
4-(cyclopropylmethoxy)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(prop-2-yn-1-yloxy)pyridine-3-carboxamide;
N-(4-((7-(azetidin-3-yloxy)-6-methoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-cyclopropoxypyridine-3-carboxamide;
4-cyclopropoxy-*N*-(4-((7-(2-(ethylamino)ethoxy)-6-methoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)pyridine-3-carboxamide;

N-[2,3-difluoro-4-((6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl)oxy)phenyl]-4-propoxy-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(2,3-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 4-cyclobutoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-2,3,5-trifluorophenyl)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(2,3,5-trifluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
N-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-(2-hydroxyethoxy)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 (S)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxypropoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 (R)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxypropoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 (R)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(3-hydroxybutoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-methoxyethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-6-fluoropyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-6-methoxypyridine-3-carboxamide;
 6-chloro-4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-6-methylpyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-6-methylpyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-2-fluoropyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxy-2-fluoropyridine-3-carboxamide;

N-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-{[6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-{[6-(2-hydroxypropoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*R*)-*N*-(3,5-difluoro-4-{[6-(2-hydroxypropoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-{[6-(2-hydroxy-2-methylpropoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-{[6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-((7-methoxy-6-((1-methoxypropan-2-yl)oxy)quinolin-4-yl)oxy)phenyl)-4-methoxynicotinamide;

(*S*)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl)oxy)phenyl)nicotinamide;

(*R*)-*N*-(3,5-difluoro-4-{[6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-(1-(hydroxymethyl)cyclopropoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxynicotinamide;

(*S*)-4-methoxy-*N*-(2,3,5-trifluoro-4-((6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl)oxy)phenyl)nicotinamide;

N-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)-2-fluoropyridine-3-carboxamide;

N-(3,5-difluoro-4-(((6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)-2-fluoropyridine-3-carboxamide; and

N-(3,5-difluoro-4-(((6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)pyridine-3-carboxamide.

[0002d] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound, or pharmaceutically acceptable salt or solvate thereof, as described herein and a pharmaceutically acceptable excipient

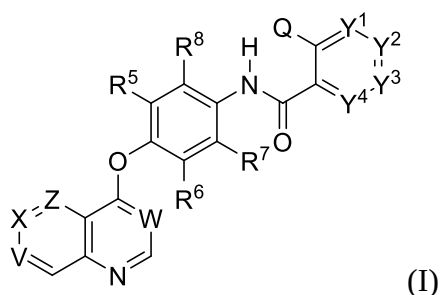
[0002e] In a further aspect of the present disclosure, there is provided a use of a compound as described herein, or pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating cancer in a patient in need thereof.

[0002f] In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition comprising a compound as described herein, or pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient, in the manufacture of a medicament for treating cancer in a patient in need thereof.

[0002g] In a further aspect of the present disclosure, there is provided a compound as described herein, or pharmaceutically acceptable salt or solvate thereof, or a pharmaceutical composition comprising a compound as described herein, or pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient, for use in therapy.

[0003] Provided herein are inhibitors of MET kinase, pharmaceutical compositions comprising said inhibitory compounds, and methods for using said inhibitory compounds for the treatment of disease.

[0004] One example provides a compound, or a pharmaceutically acceptable salt or solvate thereof, having the structure of Formula (I):



wherein,

V is independently N or C-L-R;

X is independently N, or C-L¹-R¹;

Z is N or C-R²; provided that V, X, and Z are not all N;

substituted C3-C6 cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclylalkyl.

[0005] One example provides a pharmaceutical composition comprising a compound of Formula (I), or pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

[0006] One example provides a method of treating a disease or disorder in a patient in need thereof comprising administering to the patient a compound of Formula (I), or pharmaceutically acceptable salt or solvate thereof. Another example provides the method wherein the disease or disorder is cancer.

INCORPORATION BY REFERENCE

[0007] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference for the specific purposes identified herein.

DETAILED DESCRIPTION OF THE INVENTION

[0008] As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an agent" includes a plurality of such agents, and reference to "the cell" includes reference to one or more cells (or to a plurality of cells) and equivalents thereof known to those skilled in the art, and so forth. When ranges are used herein for physical properties, such as molecular weight, or chemical properties, such as chemical formulae, all combinations and subcombinations of ranges and specific embodiments therein are intended to be included. The term "about" when referring to a number or a numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and thus the number or numerical range, in some instances, will vary between 1% and 15% of the stated number or numerical range. The term "comprising" (and related terms such as "comprise" or "comprises" or "having" or "including") is not intended to exclude that in other certain embodiments, for example, an embodiment of any composition of matter, composition, method, or process, or the like, described herein, "consist of" or "consist essentially of" the described features.

Definitions

[0009] As used in the specification and appended claims, unless specified to the contrary, the following terms have the meaning indicated below.

[0010] "Amino" refers to the -NH_2 radical.

[0011] "Cyano" refers to the -CN radical.

[0012] "Nitro" refers to the -NO_2 radical.

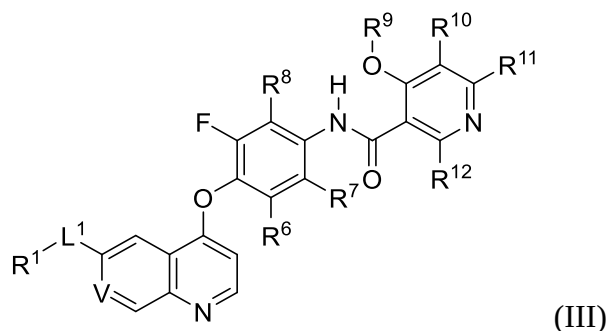
We claim:

R1Lc1ccc2c(c1)c(c[nH]2)Oc3cc(F)c(NC(=O)c4cc(R10)c(R11)c(R12)n4)c(R8)c3R7 (II)

R¹² is H, halogen, -NH₂, -CN, optionally substituted C1-C6 alkyl or optionally

substituted C1-C6 alkoxy.

2. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein X is C-L¹-R¹.
3. The compound of claim 2, or a pharmaceutically acceptable salt or solvate thereof, wherein L¹ is -O-.
4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein R¹ is optionally substituted C1-C6 alkyl.
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein R¹ is optionally substituted C1-C2 alkyl.
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt or solvate thereof, wherein R¹ is optionally substituted C1 alkyl.
7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt or solvate thereof, wherein L is -O-.
8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt or solvate thereof, wherein R is optionally substituted C1-C6 alkyl.
9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt or solvate thereof, wherein R is optionally substituted C1-C2 alkyl.
10. A compound, or a pharmaceutically acceptable salt or solvate thereof, having the structure of Formula (III):



wherein,

V is independently N or C-L-R;

L is a bond, -O-, -NH-, -NHCO-, or -CONH-;

L¹ is a bond, -O-, -NH-, -NHCO-, or -CONH-;

R is selected from the group consisting of H, halogen, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkenyl, optionally substituted C1-C6 alkynyl, optionally substituted C3-C6 cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heteroaryl, and optionally substituted heteroarylalkyl;

R¹ is selected from the group consisting of H, halogen, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkenyl, optionally substituted C1-C6 alkynyl, optionally substituted C3-C6 cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclalkyl, optionally substituted heteroaryl, and optionally substituted heteroarylalkyl;

R⁶, R⁷ and R⁸ are each independently selected from H or halogen; provided that at least one of R⁶, R⁷ or R⁸ is not H;

R⁹ is selected from the group consisting of optionally substituted C1-C6 alkyl, optionally substituted C3-C6 cycloalkyl, and optionally substituted cycloalkylalkyl;

R¹⁰ is H;

R¹¹ is H, halogen, -NH₂, -CN, optionally substituted C1-C6 alkyl, optionally substituted C1-C6 alkoxy, -NH(optionally substituted C1-C6 alkyl), or -N(optionally substituted C1-C6 alkyl)₂;

R¹² is H, halogen, optionally substituted C1-C6 alkyl or optionally substituted C1-C6 alkoxy.

11. The compound of claim 10, or a pharmaceutically acceptable salt or solvate thereof, wherein V is C-L-R.

12. The compound of claim 11, or a pharmaceutically acceptable salt or solvate thereof, wherein L is -O-.

13. The compound of any one of claims 10 to 12, or a pharmaceutically acceptable salt or solvate thereof, wherein R is optionally substituted C1-C6 alkyl.

14. The compound of any one of claims 10 to 13, or a pharmaceutically acceptable salt or solvate thereof, wherein R is optionally substituted C1-C2 alkyl.

15. The compound of any one of claims 10 to 14, or a pharmaceutically acceptable salt or solvate thereof, wherein R is optionally substituted C1 alkyl.

16. The compound of any one of claims 10-15, or a pharmaceutically acceptable salt or solvate thereof, wherein L^1 is -O-.
17. The compound of any one of claims 10-16, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is optionally substituted C1-C6 alkyl.
18. The compound of any one of claims 10-17, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is optionally substituted C1-C6 alkyl.
19. The compound of any one of claims 10-18, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is optionally substituted C1 alkyl.
20. The compound of any one of claims 10-19, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is CH_3 .
21. The compound of any one of claims 10 to 16, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is optionally substituted C3-C6 cycloalkyl.
22. The compound of claim 21, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is optionally substituted cyclopropyl.
23. A compound, or pharmaceutically acceptable salt or solvate thereof, selected from the group consisting of:
N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
6-chloro-*N*-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide formate;
N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-ethoxypyridine-3-carboxamide;
N-(3-chloro-5-fluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinazolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinazolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-2-fluoro-4-methoxypyridine-3-carboxamide;
N-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-ethoxypyridine-3-carboxamide;
N-(2,3-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxypyridine-3-carboxamide;
N-(2,3-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxypyridine-3-carboxamide;
N-(2,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;
N-(4-((7-(3-(dimethylamino)propoxy)-6-methoxyquinolin-4-yl)oxy)-2,5-difluorophenyl)-4-ethoxypyridine-3-carboxamide;
N-[2,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-(2,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-2-fluoro-4-methoxypyridine-3-carboxamide;
6-chloro-*N*-[2,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-[2,5-difluoro-4-({6-methoxy-7-[3-(morpholin-4-yl)propoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxypyridine-3-carboxamide;
N-[3,5-difluoro-4-({6-methoxy-7-[2-(morpholin-4-yl)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;
N-(3,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

6-amino-*N*-(2,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

6-amino-*N*-[2,5-difluoro-4-({6-methoxy-7-[3-(morpholin-4-yl)propoxy]quinolin-4-yl}oxy)phenyl]-4-ethoxypyridine-3-carboxamide;

6-amino-*N*-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;

N-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(trifluoromethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-(4-((7-(difluoromethoxy)-6-methoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((7-(2-hydroxy-2-methylpropoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-(4-((6,7-bis(2-methoxyethoxy)quinolin-4-yl)oxy)-3,5-difluorophenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-6-fluoro-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxy-6-methylpyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-methoxy-6-((2-methoxyethyl)amino)pyridine-3-carboxamide;

N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-(difluoromethoxy)pyridine-3-carboxamide;

N-(2,3-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(difluoromethoxy)pyridine-3-carboxamide;

4-methoxy-*N*-[2,3,5-trifluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]pyridine-3-carboxamide;

4-ethoxy-*N*-(2,3,5-trifluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

N-[2,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-propoxypyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(3-morpholinopropoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

4-cyclopropoxy-*N*-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]pyridine-3-carboxamide;

4-cyclobutoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-propoxy-pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(3,3-difluorocyclobutoxy)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(3-fluoropropoxy)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-isopropoxy-pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)pyridine-3-carboxamide;

(*R*)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-fluoropropoxy)pyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-fluoropropoxy)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxyethoxy)pyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxypropoxy)pyridine-3-carboxamide;

(*R*)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxypropoxy)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-hydroxy-2-methylpropoxy)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(2-methoxyethoxy)pyridine-3-carboxamide;

4-butoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

4-(cyclopropylmethoxy)-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-4-(prop-2-yn-1-yloxy)pyridine-3-carboxamide;

N-(4-((7-(azetidin-3-yloxy)-6-methoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-cyclopropoxy-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(4-((7-(2-(ethylamino)ethoxy)-6-methoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-pyridine-3-carboxamide;
N-[2,3-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-propoxy-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(2,3-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 4-cyclobutoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-2,3,5-trifluorophenyl)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(2,3,5-trifluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
N-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-4-(2-hydroxyethoxy)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 (S)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxypropoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 (R)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxypropoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 (R)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(3-hydroxybutoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-methoxyethoxy)quinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-pyridine-3-carboxamide;
 4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-6-fluoropyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-6-methoxypyridine-3-carboxamide;

6-chloro-4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-6-methylpyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-methoxy-7-(2-(methylamino)ethoxy)quinolin-4-yl)oxy)phenyl)-6-methylpyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-2-fluoropyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-methoxy-7-(3-(methylamino)propoxy)quinolin-4-yl)oxy)phenyl)-4-ethoxy-2-fluoropyridine-3-carboxamide;

N-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-{[6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-{[6-(2-hydroxypropoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*R*)-*N*-(3,5-difluoro-4-{[6-(2-hydroxypropoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-{[6-(2-hydroxy-2-methylpropoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-{[6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-((7-methoxy-6-((1-methoxypropan-2-yl)oxy)quinolin-4-yl)oxy)phenyl)-4-methoxynicotinamide;

(*S*)-4-cyclopropoxy-*N*-(3,5-difluoro-4-((6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl)oxy)phenyl)nicotinamide;

(*R*)-*N*-(3,5-difluoro-4-{[6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-(1-(hydroxymethyl)cyclopropoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxynicotinamide;

(*S*)-4-methoxy-*N*-(2,3,5-trifluoro-4-((6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl)oxy)phenyl)nicotinamide;

N-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)-2-fluoropyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)-2-fluoropyridine-3-carboxamide; and

N-(3,5-difluoro-4-((6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-(2,2-difluoroethoxy)pyridine-3-carboxamide.

24. The compound of claim 23, or pharmaceutically acceptable salt or solvate thereof, wherein the compound is selected from the group consisting of:

N-[3,5-difluoro-4-({6-methoxy-7-[2-(methylamino)ethoxy]quinolin-4-yl}oxy)phenyl]-4-methoxypyridine-3-carboxamide;

N-(3,5-difluoro-4-{[6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

4-cyclopropoxy-*N*-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)pyridine-3-carboxamide;

(*S*)-*N*-(3,5-difluoro-4-{[6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide;

4-cyclopropoxy-*N*-(4-((6,7-dimethoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)pyridine-3-carboxamide;

N-(3,5-difluoro-4-((6-(1-(hydroxymethyl)cyclopropoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxynicotinamide; and

N-(3,5-difluoro-4-((7-(2-hydroxyethoxy)-6-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxypyridine-3-carboxamide.

25. The compound of claim 24, or pharmaceutically acceptable salt or solvate thereof, wherein the compound is (*S*)-*N*-(3,5-difluoro-4-{[6-((1-hydroxypropan-2-yl)oxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide.

26. The compound of claim 24, or pharmaceutically acceptable salt or solvate thereof, wherein the compound is *N*-(3,5-difluoro-4-{[6-(2-hydroxyethoxy)-7-methoxyquinolin-4-yl]oxy}phenyl)-4-methoxypyridine-3-carboxamide.

27. The compound of claim 24, or pharmaceutically acceptable salt or solvate thereof, wherein the compound is *N*-(3,5-difluoro-4-((6-(1-(hydroxymethyl)cyclopropoxy)-7-methoxyquinolin-4-yl)oxy)phenyl)-4-methoxynicotinamide.
28. A pharmaceutical composition comprising a compound, or pharmaceutically acceptable salt or solvate thereof, as described in any one of claims 1 - 27 and a pharmaceutically acceptable excipient.
29. Use of a compound as described in any one of claims 1 - 27, or pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating cancer in a patient in need thereof.
30. Use of a pharmaceutical composition comprising a compound as described in any one of claims 1 - 27, or pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient, in the manufacture of a medicament for treating cancer in a patient in need thereof.
31. A compound as described in any one of claims 1 - 27, or pharmaceutically acceptable salt or solvate thereof, or a pharmaceutical composition comprising a compound as described in any one of claims 1 - 27, or pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient, for use in therapy.