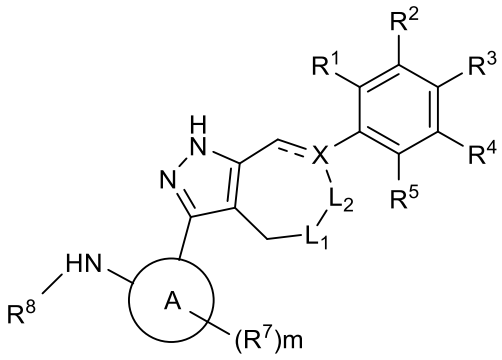
**[9]** Pathogenic elevations of bile acid levels have been linked to variations in FGF19 levels (Vergnes et al., Cell Metabolism (2013) 17, 916-28). Reduction in the level of FGF19 may therefore be of benefit in promoting the synthesis of bile acid and thus in the treatment of hyperlipidemia.

**[10]** There is still a need for new FGFR4 inhibitors. In this regard, the compounds provided herein address the need.

## BRIEF SUMMARY

**[10a]** In an aspect of the present disclosure, there is provided a compound of formula (I):




(I),

or a stereoisomer, tautomer, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

---- is a single bond or a double bond;

X is CH or C;

$L_1$ is -CR'R"-, -O-, or -NR'"-, wherein R' and R" are each independently H, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, or halo, and R'" is H, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, or acyl;

$L_2$ is a bond or -$CH_2$-;

A is a $C_{6-14}$ arylene, 5- to 10- membered heteroarylene, $C_{3-8}$ cycloalkylene, or 3- to 10- membered heterocyclylene,

provided that when $L_1$ is -$CH_2$- and $L_2$ is a bond, then A is 5- to 10- membered heteroarylene, $C_{3-8}$ cycloalkylene, or 3- to 10- membered heterocyclylene;

$R^1$, $R^2$, $R^3$, $R^4$, and $R^5$ are each independently H, halo, -CN, -$NO_2$, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-8}$ cycloalkyl, -$OR^{13}$, or -$NR^{11}R^{12}$,

or $R^1$ and X are taken together with the carbons to which they are attached to form a 4- to 8- membered heterocyclyl;

m is 0, 1, or 2;

each $R^7$ is independently halo, -CN, -$NO_2$, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-8}$ cycloalkyl, -$OR^{13}$, or -$NR^aR^b$, wherein $R^a$ and $R^b$ are each independently H or $C_{1-6}$ alkyl optionally substituted by -$NR^cR^d$, wherein $R^c$ and $R^d$ are each independently H or $C_{1-6}$ alkyl;

$R^8$ is –$C(O)R^9$ or –$S(O)_2R^9$;

$R^9$ is $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{3-8}$ cycloalkyl, or 3- to 10- membered heterocyclyl, each of which is optionally substituted with $C_{1-6}$ alkyl, halo, -CN, or –$C(O)OR^{9a}$, wherein $R^{9a}$ is $C_{1-6}$ alkyl; and

$R^{11}$, $R^{12}$, and $R^{13}$ are each independently H, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ heteroalkyl, $C_{6-14}$ aryl, 5- to 10- membered heteroaryl, $C_{3-8}$ cycloalkyl, or 3- to 10- membered heterocyclyl;

provided that the compound is not a compound selected from the group consisting of:

N-(3-(6-(2,6-dichloro-3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1H-pyrazol-4-yl)acrylamide,

N-(3-(6-(2,6-dichloro-3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1-methyl-1H-pyrazol-4-yl)acrylamide,

N-(5-(6-(2,6-dichloro-3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1-methyl-1H-pyrazol-4-yl)acrylamide,

N-(5-(6-(2,6-difluoro-3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1-methyl-1H-pyrazol-4-yl)acrylamide,

N-(5-(6-(2-fluoro-3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1-methyl-1H-pyrazol-4-yl)acrylamide,

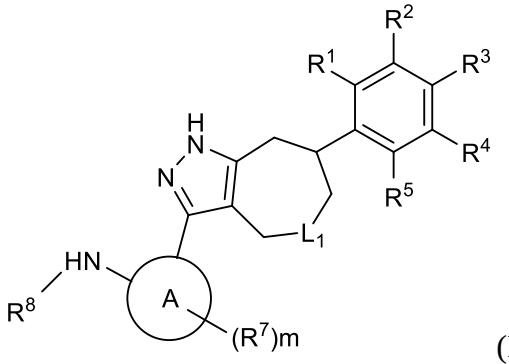
N-(5-(6-(2-chloro-6-fluoro-3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1-methyl-1H-pyrazol-4-yl)acrylamide,

N-(5-(6-(3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1-methyl-1H-pyrazol-4-yl)acrylamide, and

N-(5-(6-(2-chloro-3,5-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-indazol-3-yl)-1-methyl-1H-pyrazol-4-yl)acrylamide,

or a stereoisomer, tautomer, or a pharmaceutically acceptable salt of any of the foregoing.

**[10b]** In another aspect of the present disclosure, there is provided a compound of formula (II):




(II),

or a stereoisomer, tautomer, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

⁼⁼⁼⁼ is a single bond or a double bond;

X is CH or C;

$L_1$ is -CR'R"-, -O-, or -NR'"-, wherein R' and R" are each independently H, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, or halo, and R'" is H, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, or acyl;

$L_2$ is a bond or -$CH_2$-;

A is a $C_{6-14}$ arylene, 5- to 10- membered heteroarylene, $C_{3-8}$ cycloalkylene, or 3- to 10-membered heterocyclylene;$R^1$, $R^2$, $R^3$, $R^4$, and $R^5$ are each independently H, halo, -CN, -$NO_2$, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-8}$ cycloalkyl, -$OR^{13}$, or -$NR^{11}R^{12}$,

or $R^1$ and X are taken together with the carbons to which they are attached to form a 4- to 8- membered heterocyclyl;

m is 0, 1, or 2;

each $R^7$ is independently halo, -CN, -$NO_2$, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-8}$ cycloalkyl, -$OR^{13}$, or -$NR^aR^b$, wherein $R^a$ and $R^b$ are each independently H or $C_{1-6}$ alkyl, wherein the $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-8}$ cycloalkyl, and -$OR^{13}$ of $R^7$ and the $C_{1-6}$ alkyl of $R^a$ and $R^b$ are each independently optionally substituted by -$NR^cR^d$, wherein $R^c$ and $R^d$ are each independently H or $C_{1-6}$ alkyl;

$R^8$ is $–C(O)R^9$ or $–S(O)_2R^9$;

$R^9$ is $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{3-8}$ cycloalkyl, or 3- to 10- membered heterocyclyl, each of which is optionally substituted with $C_{1-6}$ alkyl, halo, -CN, or $–C(O)OR^{9a}$, wherein $R^{9a}$ is $C_{1-6}$ alkyl; and

$R^{11}$, $R^{12}$, and $R^{13}$ are each independently H, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ heteroalkyl, $C_{6-14}$ aryl, 5- to 10- membered heteroaryl, $C_{3-8}$ cycloalkyl, or 3- to 10- membered heterocyclyl.

**[10c]** In a further aspect of the present disclosure, there is provided a compound selected from the compounds in Table 1, or a stereoisomer, tautomer, or a pharmaceutically acceptable salt of any of the foregoing.

**[10d]** In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising at least one compound disclosed herein, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing, and a pharmaceutically acceptable carrier or excipient.

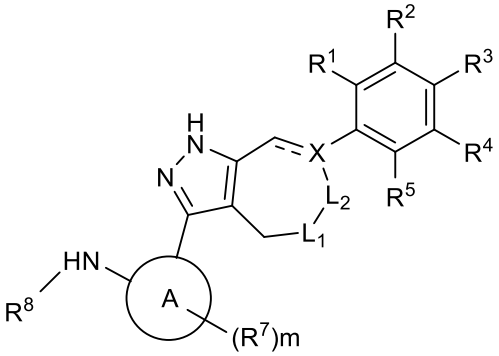
**[10e]** In a further aspect of the present disclosure, there is provided a kit comprising at least one compound disclosed herein, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing.

**[10f]** In another aspect of the present disclosure, there is provided a method of treating a disease mediated by FGFR4 in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a compound disclosed herein, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing.

**[10g]** In a further aspect of the present disclosure, there is provided a method of inhibiting FGFR4, comprising contacting FGFR4 with a compound disclosed herein, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing.

**[10h]** In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing, in the manufacture of a medicament for use in therapy.

**[11]** In one example, provided herein is a compound of formula (I):




(I),

or a stereoisomer, tautomer, or a pharmaceutically acceptable salt of any of the foregoing, wherein ----, X, $L_1$, $L_2$, A, m, $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^7$, and $R^8$ are as described herein.

**[12]** In another example, provided herein is a composition comprising a compound of formula (I) or any related formula, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing and a pharmaceutically acceptable carrier or excipient.

**[13]** In another example, provided herein is a kit comprising a compound of formula (I) or any related formula, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing.

**[14]** In another example, provided herein is a method of treating a disease mediated by FGFR4 in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a compound of formula (I) or any related formula, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing. In some examples, the compound, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing, is administered orally. In some examples, the disease is cancer. In some examples, the disease is liver cancer such as hepatocellular carcinoma,

breast cancer, rhabdomyosarcoma, or ovarian cancer. In some examples, the disease is hyperlipidemia.

**[15]** In another example, provided herein is a method of inhibition FGFR4, comprising contacting FGFR4 with a compound of formula (I) or any related formula, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing.

**[16]** In another example, provided herein is a compound of formula (I) or any related formula, or a stereoisomer, tautomer or a pharmaceutically acceptable salt of any of the foregoing, in the manufacture of a medicament for use in therapy.

## DETAILED DESCRIPTION

**[17]** Described herein are compounds, including therapeutic agents, that can inhibit FGFR4. These compounds could be used in the prevention and/or treatment of certain pathological conditions as described herein.

*Definitions*

**[18]** For use herein, unless clearly indicated otherwise, use of the terms "a", "an" and the like refers to one or more.

**[19]** Reference to "about" a value or parameter herein includes (and describes) embodiments that are directed to that value or parameter per se. For example, description referring to "about X" includes description of "X".

**[20]** "Alkyl" as used herein refers to and includes, unless otherwise stated, a saturated linear (*i.e.*, unbranched) or branched univalent hydrocarbon chain or combination thereof, having the number of carbon atoms designated (*i.e.*, $C_{1-10}$ means one to ten carbon atoms). Particular alkyl groups are those having 1 to 20 carbon atoms (a "$C_{1-20}$ alkyl"), having 1 to 10 carbon atoms (a "$C_{1-10}$ alkyl"), having 6 to 10 carbon atoms (a "$C_{6-10}$ alkyl"), having 1 to 6 carbon atoms (a "$C_{1-6}$ alkyl"), having 2 to 6 carbon atoms (a "$C_{2-6}$ alkyl"), or having 1 to 4 carbon atoms (a "$C_{1-4}$ alkyl"). Examples of alkyl groups include, but are not limited to, groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl, n-decyl, and the like.

**[21]** "Alkylene" as used herein refers to the same residues as alkyl, but having bivalency. Particular alkylene groups are those having 1 to 20 carbon atoms (a "$C_{1-20}$ alkylene"), having 1 to 10 carbon atoms (a "$C_{1-10}$ alkylene"), having 6 to 10 carbon atoms (a