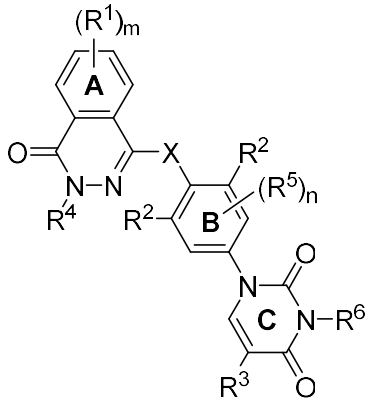
CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula **I**:



(**I**),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^1 is independently halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{3-10} carbocyclyl, or C_{6-14} aryl;

each R^2 is independently halogen, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl;

R^3 is halogen, -CN, $-NO_2$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-14} aryl, 5- to 14-membered heteroaryl, C_{3-10} carbocyclyl, 3- to 10-membered heterocyclyl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

each occurrence of R^4 and R^6 is independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-14} aryl, 5- to 14-membered heteroaryl, C_{3-10} carbocyclyl, or 3- to 10-membered heterocyclyl, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

each R^5 is independently halogen, -CN, $-NO_2$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-14} aryl, 5- to 14-membered heteroaryl, C_{3-10} carbocyclyl, 3- to 10-membered heterocyclyl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, -

$S(=O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u;

m is an integer selected from 0 to 4;

n is an integer selected from 0 to 2;

X is selected from $-C(R^7)_2-$, -O-, $-NR^8-$, and -S-;

each R^7 is independently hydrogen, halogen, -CN, $-NO_2$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-14} aryl, 5- to 14-membered heteroaryl, C_{3-10} carbocyclyl, 3- to 10-membered heterocyclyl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more R^u; and

R^8 is hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-14} aryl, 5- to 14-membered heteroaryl, C_{3-10} carbocyclyl, or 3- to 10-membered heterocyclyl, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocyclyl, or heterocyclyl is optionally substituted with one or more R^u;

wherein:

each R^u is independently halogen, -CN, $-NO_2$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-14} aryl, 5- to 14-membered heteroaryl, C_{3-10} carbocyclyl, 3- to 10-membered heterocyclyl, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2NR^cR^d$, $-NR^cR^d$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2R^a$, $-NR^cS(=O)_2OR^b$, $-NR^cS(=O)_2NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-OR^b$, $-OS(=O)_2R^a$, $-OS(=O)_2OR^b$, $-OS(=O)_2NR^cR^d$, $-OC(=O)R^a$, $-OC(=O)OR^b$, $-OC(=O)NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more oxo,

halogen, -CN, -OH, -OMe, $-NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_{1-6} alkyl, or C_{1-6} haloalkyl;

two R^u are taken together to form an oxo; or

two R^u, together with the one or more intervening atoms, form a C_{6-14} aryl, 5- to 14-membered heteroaryl, C_{3-10} carbocyclyl, or 3- to 10-membered heterocyclyl;

each R^a is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocyclyl, 3- to 10-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more oxo, halogen, -CN, -OH, -OMe, $-NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_{1-6} alkyl, or C_{1-6} haloalkyl;

each R^b is independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocyclyl, 3- to 10-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more oxo, halogen, -CN, -OH, -OMe, $-NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_{1-6} alkyl, or C_{1-6} haloalkyl; and

each R^c and R^d is independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocyclyl, 3- to 10-membered heterocyclyl, C_{6-14} aryl, or 5- to 14-membered heteroaryl, wherein the alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one or more oxo, halogen, -CN, -OH, -OMe, $-NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_{1-6} alkyl, or C_{1-6} haloalkyl;

or R^c, R^d, together with the nitrogen atom to which they are attached, form a 3- to 10-membered heterocyclyl optionally substituted with one or more oxo, halogen, -CN, -OH, -OMe, $-NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_{1-6} alkyl, or C_{1-6} haloalkyl.

2. The compound of claim 1, wherein each R^1 is independently halogen, C_{1-6} alkyl, C_{1-6} alkoxy, or C_{6-14} aryl.

3. The compound of claim 1 or 2, wherein m is 0, 1, or 2.

4. The compound of any one of claims 1-3, wherein each R^2 is independently halogen or C_{1-6} alkyl.

5. The compound of any one of claims 1-4, wherein each R^2 is halogen.

6. The compound of any one of claims 1-5, wherein each R^2 is chloride.

7. The compound of any one of claims 1-6, wherein R^3 is -CN, $-C(=O)OR^b$, or $-C(=O)NR^cR^d$.

8. The compound of any one of claims 1-7, wherein R^3 is -CN.

9. The compound of any one of claims 1-7, wherein each R^c and R^c is H.

10. The compound of any one of claims 1-7, wherein R^3 is $-C(=O)NH_2$.

11. The compound of any one of claims 1-7, wherein R^b is H.

12. The compound of any one of claims 1-7, wherein R^3 is -C(=O)OH.

13. The compound of any one of claims 1-12, wherein R^4 is hydrogen.

14. The compound of any one of claims 1-13, wherein n is 0.

15. The compound of any one of claims 1-14, wherein R^6 is hydrogen.

16. The compound of any one of claims 1-15, wherein X is O.

17. The compound of claim 1, wherein the compound is selected from the compounds described in Table I, and pharmaceutically acceptable salts, stereoisomers, and solvates thereof.

18. A pharmaceutical composition comprising a compound of any one of claims 1-17, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, and a pharmaceutically acceptable excipient.

19. A method of activating thyroid hormone receptor (THR) β in a patient or a biological sample, the method comprising contacting the patient or biological sample with a compound of any one of claims 1-17, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof.

20. Use of a compound of any one of claims 1-17, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, in the manufacture of a medicament for treating a liver disease or disorder, or a lipid disease or disorder.

21. The use of claim 20, wherein the liver disease or disorder is nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), or fatty liver disease.

22. The use of claim 20, wherein the lipid disease or disorder is dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low high-density lipoprotein (HDL), or high low-density lipoprotein (LDL).

23. The use of claim 22, wherein hypercholesterolemia is heterozygous familial hypercholesterolemia (HeFH) or homozygous familial hypercholesterolemia (HoFH).