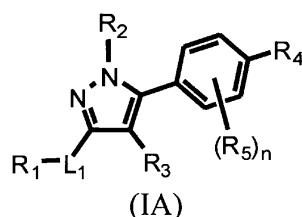


embodiment is a compound of Formula I wherein R_1 is $-\text{CF}_3$. In another embodiment is a compound of Formula I wherein R_1 is $-\text{C}(=\text{O})\text{R}_8$. In another embodiment is a compound of Formula I wherein R_1 is $-\text{C}(=\text{O})\text{R}_8$, and R_8 is $\text{C}_1\text{-C}_6$ alkyl. In another embodiment is a compound of Formula I wherein R_1 is $\text{C}(=\text{O})\text{N}(\text{R}_9)_2$. In another embodiment of the aforementioned

5 embodiments is a compound of Formula I wherein R_2 is $\text{C}_1\text{-C}_6$ alkyl. In another embodiment of the aforementioned embodiments is a compound of Formula I wherein R_2 is isobutyl. In another embodiment of the aforementioned embodiments is a compound of Formula I wherein R_3 is hydrogen. In another embodiment of the aforementioned embodiments is a compound of Formula I wherein R_3 is halogen.

10 In one aspect is a compound of Formula (IA):



or a pharmaceutically acceptable salt thereof, wherein:

L_1 is a bond, $\text{C}_1\text{-C}_6$ alkyl, or $\text{C}_1\text{-C}_6$ heteroalkyl;

R_1 is $-\text{OR}_9$, $-\text{N}(\text{R}_9)_2$, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_1\text{-C}_6$ haloalkyl, $-\text{C}(=\text{O})\text{R}_8$, or $-\text{C}(=\text{O})\text{N}(\text{R}_9)_2$;

R_2 is $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_3\text{-C}_8$ cycloalkyl, or $-\text{C}_1\text{-C}_6$ alkyl- $\text{C}_3\text{-C}_8$ cycloalkyl;

R_3 is hydrogen, halogen, $\text{C}_1\text{-C}_6$ alkyl, or $\text{C}_1\text{-C}_6$ haloalkyl;

R_4 is phenyl, which is substituted with at least one R_{11} ;

each R_5 is independently halogen, $\text{C}_1\text{-C}_6$ alkyl, or $\text{C}_1\text{-C}_6$ haloalkyl;

R_8 is $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_1\text{-C}_6$ haloalkyl, $-\text{C}_1\text{-C}_6$ alkyl-aryl, aryl, or heteroaryl;

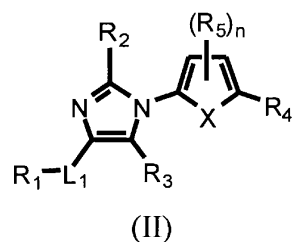
each R_9 is independently hydrogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ heteroalkyl, $\text{C}_1\text{-C}_6$ haloalkyl, aryl, or heteroaryl;

each R_{10} is independently hydrogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ heteroalkyl, $-\text{C}_1\text{-C}_6$ alkyl-aryl, aryl, or heteroaryl;

each R_{11} is independently halogen, nitro, $-\text{OR}_{10}$, $-\text{N}(\text{R}_{10})_2$, $-\text{CN}$, $-\text{C}(=\text{O})\text{R}_{10}$, $-\text{C}(=\text{O})\text{OR}_{10}$, $-\text{C}(=\text{O})\text{N}(\text{R}_{10})_2$, $-\text{NR}_{10}\text{C}(=\text{O})\text{R}_{10}$, $-\text{NR}_{10}\text{SO}_2\text{R}_{10}$, $-\text{SOR}_{10}$, $-\text{SO}_2\text{R}_{10}$, $-\text{SO}_2\text{N}(\text{R}_{10})_2$, $-\text{C}(=\text{O})\text{OCH}_2\text{SCH}_3$, optionally substituted $\text{C}_1\text{-C}_6$ alkyl, optionally substituted $\text{C}_3\text{-C}_8$ cycloalkyl, optionally substituted $\text{C}_1\text{-C}_6$ haloalkyl, optionally substituted $\text{C}_1\text{-C}_6$ heteroalkyl, optionally substituted $-\text{C}_1\text{-C}_6$ alkyl-aryl, optionally substituted aryl, or optionally substituted heteroaryl, wherein at least one R_{11} is $-\text{NR}_{10}\text{SO}_2\text{R}_{10}$, $-\text{SOR}_{10}$, $-\text{SO}_2\text{R}_{10}$, or $-\text{SO}_2\text{N}(\text{R}_{10})_2$; and

n is 0-4.

Disclosed is a compound of Formula (II):



or a pharmaceutically acceptable salt thereof, wherein:

5 X is -O-, -S-, or -C(R₆)=C(R₆)-;

L₁ is a bond, C₁-C₆alkyl, or C₁-C₆heteroalkyl;

R₁ is -OR₉, -N(R₉)₂, C₁-C₆alkyl, C₂-C₆alkenyl, C₁-C₆haloalkyl, C₂-C₉heterocycloalkyl, -C(=O)R₈, or -C(=O)N(R₉)₂;

R₂ is C₁-C₆alkyl, C₂-C₆alkenyl, C₃-C₈cycloalkyl, or -C₁-C₆alkyl-C₃-C₈cycloalkyl;

10 R₃ is hydrogen, halogen, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R₄ is aryl or heteroaryl; wherein aryl or heteroaryl is substituted with at least one R₁₁;

each R₅ is independently halogen, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R₆ is independently hydrogen, halogen, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R₈ is C₁-C₆alkyl, C₂-C₆alkenyl, C₁-C₆haloalkyl, -C₁-C₆alkyl-aryl, aryl, or heteroaryl;

15 each R₉ is independently hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, C₁-C₆haloalkyl, -C₁-C₆alkyl-aryl, aryl, or heteroaryl;

each R₁₀ is independently hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, -C₁-C₆alkyl-aryl, aryl, or heteroaryl;

mesylate, or nilotinib hydrochloride monohydrate; or a combination thereof. In some embodiments of the aforementioned embodiments the mammal is a human.

In some embodiments is a method of treating a disease, disorder or condition in a mammal that would benefit from LXR modulation comprising administering to the mammal a compound of Formula I, IA, IB, IC, II, IIA, or IIB, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate, or pharmaceutically acceptable prodrug thereof; wherein the disease, disorder or condition in a mammal is Alzheimer's disease.

In some embodiments is a method of treating a disease, disorder or condition in a mammal that would benefit from LXR modulation comprising administering to the mammal a compound of Formula I, IA, IB, IC, II, IIA, or IIB, or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate, or pharmaceutically acceptable prodrug thereof; wherein the disease, disorder or condition in a mammal is Parkinson's disease.

In one aspect is use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease, disorder or condition in a mammal, wherein the disease, disorder or condition is increased lipid levels, increased cholesterol levels, low HDL-cholesterol, high LDL-cholesterol, atherosclerotic diseases, diabetes, non-insulin dependent diabetes mellitus, metabolic syndrome, dyslipidemia, sepsis, inflammatory diseases, infectious diseases, skin diseases, colitis, pancreatitis, cholestasis of the liver, fibrosis of the liver, psoriasis, Alzheimer's disease, Parkinson's disease, impaired/improvable cognitive function, HIV, cancer including metastatic cancer and metastatic melanoma, acute macular degeneration, or age related forms of macular degeneration (wet and dry forms).

In one embodiment is the use of a compound of Formula I, IA, IB, IC, II, IIA, or IIB in the manufacture of a medicament for the treatment of a disease, disorder, or condition that would benefit from LXR modulation (such as any of the methods described herein). In another embodiment is a compound of Formula I, IA, IB, IC, II, IIA, or IIB for use in the any of the methods described herein. In another embodiment is the use of a LXR modulator in the manufacture of a medicament for use in the treatment of a disease, disorder or condition in a mammal, wherein the disease, disorder or condition in a mammal is increased lipid levels, increased cholesterol levels, low HDL-cholesterol, high LDL-cholesterol, atherosclerotic diseases, diabetes, non-insulin dependent diabetes mellitus, metabolic syndrome, dyslipidemia, sepsis, inflammatory diseases, infectious diseases, skin diseases, colitis, pancreatitis, cholestasis of the liver, fibrosis of the liver, psoriasis, Alzheimer's disease, Parkinson's disease, impaired/improvable cognitive function, HIV, cancer including metastatic cancer and metastatic melanoma, acute macular degeneration, and age related forms of macular degeneration (wet and dry forms). In another embodiment is the use of a LXR modulator and a second therapeutic agent in the manufacture of a medicament for use in the treatment of a disease, disorder or condition in a mammal, wherein the disease, disorder or condition in a mammal is increased lipid levels, increased cholesterol levels, low HDL-cholesterol, high LDL-cholesterol, atherosclerotic diseases, diabetes, non-insulin dependent diabetes mellitus, metabolic syndrome, dyslipidemia,

sepsis, inflammatory diseases, infectious diseases, skin diseases, colitis, pancreatitis, cholestasis of the liver, fibrosis of the liver, psoriasis, Alzheimer's disease, Parkinson's disease, impaired/improvable cognitive function, HIV, cancer including metastatic cancer and metastatic melanoma, and age related forms of macular degeneration (wet and dry forms).

5 In one aspect is an *in vitro* method of modulating LXR activity comprising contacting LXR, or portion thereof, with a compound as defined herein, or a pharmaceutically acceptable salt thereof.

In one embodiment is a method of modulating LXR activity comprising contacting LXR, or portion thereof, with a compound of Formula I, IA, IB, IC, II, IIA, or IIB, or a
10 pharmaceutically acceptable salt, pharmaceutically acceptable solvate, or pharmaceutically acceptable prodrug thereof.

Disclosed is use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for modulating LXR activity, wherein the compound, or pharmaceutically acceptable salt thereof, is to be contacted with LXR.

15 INCORPORATION BY REFERENCE

All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE FIGURES

20 **Figure 1** shows ABCA1 gene expression analyzed by QT-PCR for Compound 4 as outlined in Example 13.

Figure 2 shows ABCG1 gene expression analyzed by QT-PCR for Compound 4 as outlined in Example 13.

25 **Figure 3** shows IL1 β gene expression analyzed by QT-PCR for Compound 4 as outlined in Example 14.

Figure 4 shows α Syn gene expression analyzed by QT-PCR for Compound 4 as outlined in Example 15.

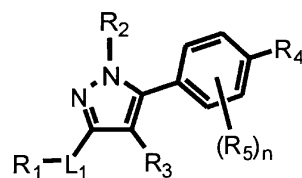
DETAILED DESCRIPTION OF THE INVENTION

Metastatic Melanoma

30 Expression levels of certain micro RNAs (miRNAs), including miRNA-1908, miRNA-199a-5p and miRNA-199a-3p and ApoE, including ApoE3 and ApoE4, correlate with the progression of malignant melanomas and metastatic disease as well as frequencies in other cancers (Tavazoie, S.F., et al., *Cell* (2012) 151:1-15). The discovery that the three miRNAs combinatorially target metastatic melanoma suppression establishes their potential as melanoma

WHAT IS CLAIMED IS:

1. A compound of Formula (IA):



(IA)

or a pharmaceutically acceptable salt thereof, wherein:

L₁ is a bond, C₁-C₆alkyl, or C₁-C₆heteroalkyl;

R₁ is -OR₉, -N(R₉)₂, C₁-C₆alkyl, C₂-C₆alkenyl, C₁-C₆haloalkyl, -C(=O)R₈, or -C(=O)N(R₉)₂;

R₂ is C₁-C₆alkyl, C₂-C₆alkenyl, C₃-C₈cycloalkyl, or -C₁-C₆alkyl-C₃-C₈cycloalkyl;

R₃ is hydrogen, halogen, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R₄ is phenyl, which is substituted with at least one R₁₁;

each R₅ is independently halogen, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R₈ is C₁-C₆alkyl, C₂-C₆alkenyl, C₁-C₆haloalkyl, -C₁-C₆alkyl-aryl, aryl, or heteroaryl;

each R₉ is independently hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, C₁-C₆haloalkyl, -aryl, or heteroaryl;

each R₁₀ is independently hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, -C₁-C₆alkyl-aryl, aryl, or heteroaryl;

each R₁₁ is independently halogen, nitro, -OR₁₀, -N(R₁₀)₂, -CN, -C(=O)R₁₀, -C(=O)OR₁₀, -C(=O)N(R₁₀)₂, -NR₁₀C(=O)R₁₀, -NR₁₀SO₂R₁₀, -SOR₁₀, -SO₂R₁₀, -SO₂N(R₁₀)₂, -

C(=O)OCH₂SCH₃, optionally substituted C₁-C₆alkyl, optionally substituted C₃-C₈cycloalkyl,

optionally substituted C₁-C₆haloalkyl, optionally substituted C₁-C₆heteroalkyl, optionally

substituted -C₁-C₆alkyl-aryl, optionally substituted aryl, or optionally substituted heteroaryl,

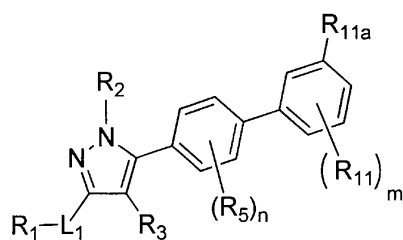
wherein at least one R₁₁ is -NR₁₀SO₂R₁₀, -SOR₁₀, -SO₂R₁₀, or -SO₂N(R₁₀)₂; and

n is 0-4.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein L₁ is a bond.

3. The compound of any one of claims 1-2, or a pharmaceutically acceptable salt thereof, wherein R_1 is C_1 - C_6 alkyl.
4. The compound of any one of claims 1-2, or a pharmaceutically acceptable salt thereof, wherein R_1 is C_2 - C_6 alkenyl.
5. The compound of any one of claims 1-2, or a pharmaceutically acceptable salt thereof, wherein R_1 is C_1 - C_6 haloalkyl.
6. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein R_1 is $-CF_3$.
7. The compound of any one of claims 1-2, or a pharmaceutically acceptable salt thereof, wherein R_1 is $-C(=O)N(R_9)_2$.
8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein L_1 is C_1 - C_6 alkyl; and R_1 is $-OH$.
9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein $-L_1-R_1$ is $-C(=CH_2)CH_3$, isopropyl, $-C(=O)NHCH_2CF_3$, $-CF_3$, or $-C(CH_3)_2OH$.
10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein R_2 is C_1 - C_6 alkyl.
11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein R_2 is isobutyl.
12. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein R_2 is sec-butyl.
13. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein R_2 is C_3 - C_8 cycloalkyl.
14. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein R_2 is $-C_1$ - C_6 alkyl- C_3 - C_8 cycloalkyl.

15. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein R_2 is isobutyl, sec-butyl, cyclohexyl, $-\text{CH}_2\text{-cyclohexyl}$, or $-\text{CH}_2\text{-cyclopropyl}$.
16. The compound of any one of claims 1-15, or a pharmaceutically acceptable salt thereof, wherein R_3 is hydrogen.
17. The compound of any one of claims 1-16, or a pharmaceutically acceptable salt thereof, wherein n is 0.
18. The compound of any one of claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R_4 is phenyl, which is substituted with at least one R_{11} .
19. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt thereof, wherein at least one R_{11} is $-\text{SO}_2R_{10}$.
20. The compound of any one of claims 19, or a pharmaceutically acceptable salt thereof, wherein each R_{10} is independently $\text{C}_1\text{-C}_6\text{alkyl}$.
21. The compound of any one of claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R_4 is phenyl substituted with one R_{11} , wherein R_{11} is $-\text{SO}_2R_{10}$ and R_{10} is $\text{C}_1\text{-C}_6\text{alkyl}$; or R_4 is phenyl substituted with two R_{11} , and one R_{11} is $-\text{SO}_2R_{10}$; and one R_{11} is optionally substituted $\text{C}_1\text{-C}_6\text{alkyl}$.
22. The compound of any one of claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R_4 is phenyl substituted with two R_{11} , wherein one R_{11} is $-\text{SO}_2\text{CH}_3$ and one R_{11} is $-\text{CH}_2\text{OH}$.
23. The compound of any one of claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R_4 is phenyl substituted with one R_{11} , wherein R_{11} is $-\text{SO}_2R_{10}$ and R_{10} is $\text{C}_1\text{-C}_6\text{alkyl}$.
24. The compound of any one of claims 1-17, wherein the compound is a compound of Formula (IB):



(IB)

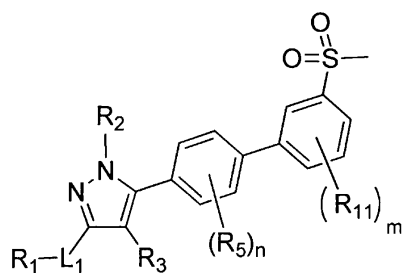
wherein:

R_{11a} is $-NR_{10}SO_2R_{10}$, $-SOR_{10}$, $-SO_2R_{10}$, or $-SO_2N(R_{10})_2$; and

m is 0 or 1;

or a pharmaceutically acceptable salt thereof.

25. The compound of any one of claims 1-17, wherein the compound is a compound of Formula (IC):



(IC)

wherein m is 0 or 1;

or a pharmaceutically acceptable salt thereof.

26. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

L_1 is a bond or C_1 - C_6 alkyl;

R_1 is $-OR_9$, $-C_1$ - C_6 alkyl, C_2 - C_6 alkenyl, C_1 - C_6 haloalkyl, or $-C(=O)N(R_9)_2$;

R_2 is C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, or $-C_1$ - C_6 alkyl- C_3 - C_8 cycloalkyl;

R_3 is hydrogen;

R_4 is phenyl substituted with at least one R_{11} ;

each R_{11} is independently $-NR_{10}SO_2R_{10}$, $-SOR_{10}$, $-SO_2R_{10}$, $-SO_2N(R_{10})_2$, or C_1 - C_6 alkyl,

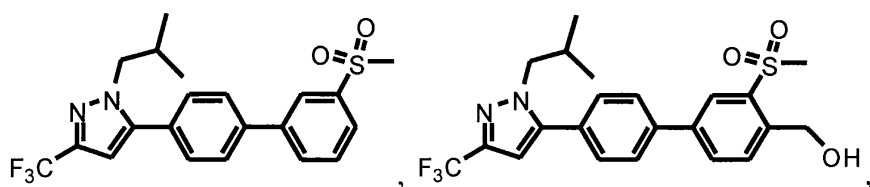
wherein said C_1 - C_6 alkyl is optionally substituted by 1 hydroxy;

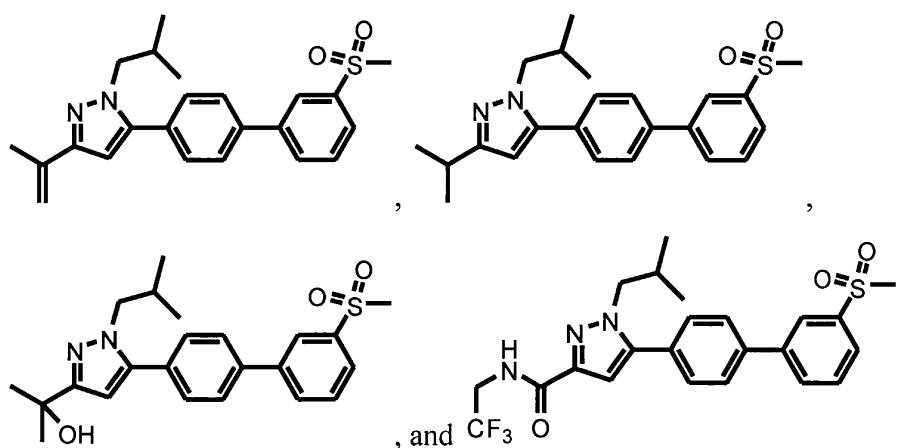
provided that at least one R_{11} is $-NR_{10}SO_2R_{10}$, $-SOR_{10}$, $-SO_2R_{10}$, or $-SO_2N(R_{10})_2$,
each R_{10} is independently C_1 - C_6 alkyl; and
each R_9 is independently hydrogen or C_1 - C_6 haloalkyl; and
 n is 0.

27. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:
 L_1 is a bond or C_1 - C_6 alkyl;
 R_1 is $-OR_9$, $-C_1$ - C_6 alkyl, C_2 - C_6 alkenyl, C_1 - C_6 haloalkyl, or $-C(=O)N(R_9)_2$;
 R_2 is C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, or $-C_1$ - C_6 alkyl- C_3 - C_8 cycloalkyl;
 R_3 is hydrogen;
 R_4 is phenyl substituted with one R_{11} , wherein R_{11} is $-SO_2R_{10}$ and R_{10} is C_1 - C_6 alkyl; or
 R_4 is phenyl substituted with two R_{11} , wherein one R_{11} is $-SO_2R_{10}$ and one R_{11} is
optionally substituted C_1 - C_6 alkyl;
each R_9 is independently hydrogen or C_1 - C_6 haloalkyl; and
 n is 0.

28. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:
 $-L_1-R_1$ is $-C(=CH_2)CH_3$, isopropyl, $-C(=O)NHCH_2CF_3$, $-CF_3$, or $-C(CH_3)_2OH$;
 R_2 is isobutyl, sec-butyl, cyclohexyl, $-CH_2$ -cyclohexyl, or $-CH_2$ -cyclopropyl;
 R_3 is hydrogen;
 R_4 is phenyl substituted with two R_{11} , wherein one R_{11} is $-SO_2CH_3$ and one R_{11} is $-CH_2OH$; or R_4 is phenyl substituted with one R_{11} , wherein R_{11} is $-SO_2R_{10}$ and R_{10} is CH_3 ; and
 n is 0.

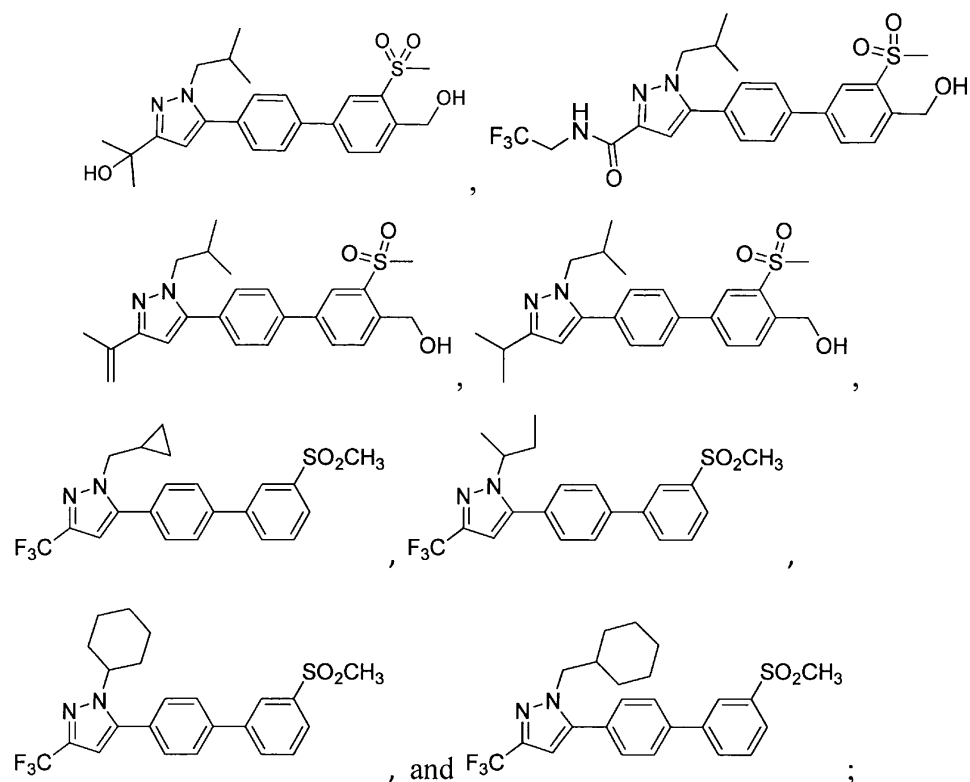
29. The compound of claim 1, selected from:





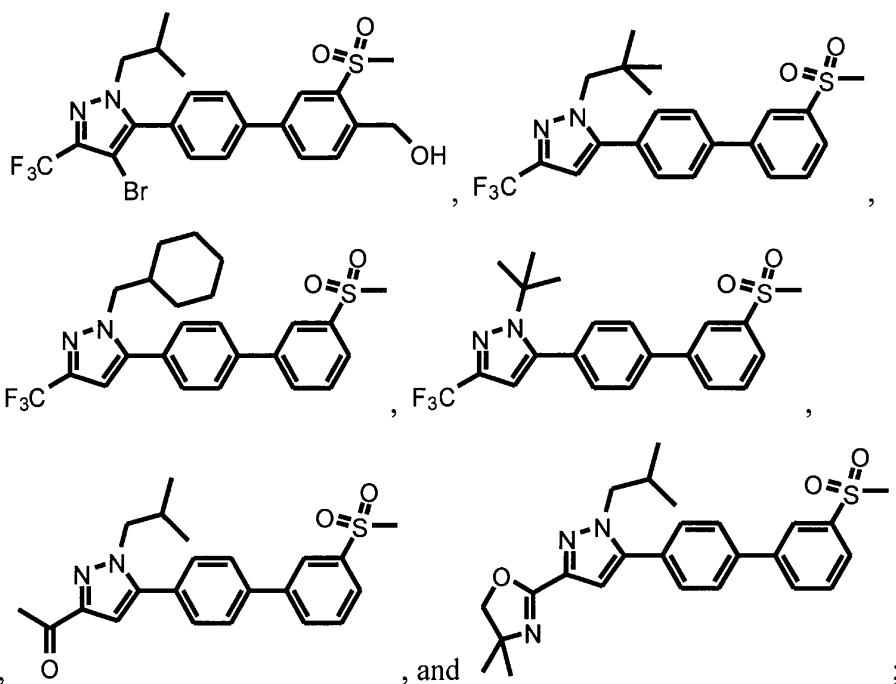
or a pharmaceutically acceptable salt thereof.

30. The compound of claim 1, selected from:



or a pharmaceutically acceptable salt thereof.

31. A compound selected from:



or a pharmaceutically acceptable salt thereof.

32. A pharmaceutical composition comprising a compound according to any one of claims 1-31, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

33. Use of a compound according to any one of claims 1-31, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease, disorder or condition in a mammal, wherein the disease, disorder or condition is increased lipid levels, increased cholesterol levels, low HDL-cholesterol, high LDL-cholesterol, atherosclerotic diseases, diabetes, non-insulin dependent diabetes mellitus, metabolic syndrome, dyslipidemia, sepsis, inflammatory diseases, infectious diseases, skin diseases, colitis, pancreatitis, cholestasis of the liver, fibrosis of the liver, psoriasis, Alzheimer's disease, Parkinson's disease, impaired/improvable cognitive function, HIV, cancer including metastatic cancer and metastatic melanoma, acute macular degeneration, or age related forms of macular degeneration (wet and dry forms).

34. The use of claim 33, wherein the disease, disorder or condition is cancer.

35. The use of claim 34, wherein the cancer is malignant melanoma.

36. The use of claim 34, wherein ApoE levels are reduced in said cancer.
37. The use of claim 33, wherein the medicament is to be administered with a second therapeutic agent.
38. The use of claim 37, wherein the second therapeutic agent is a BRAF inhibitor.
39. The use of claim 38, wherein the BRAF inhibitor is selected from PDC-4032, GSK2118436, and PLX-3603.
40. The use of claim 37, wherein the second therapeutic agent is sunitinib malate, sorafenib tosylate, imatinib mesylate, or nilotinib hydrochloride monohydrate; or a combination thereof.
41. The use of any one of claims 33-40, wherein the mammal is a human.
42. The use of claim 33, wherein the disease, disorder or condition is Alzheimer's disease.
43. The use of claim 33, wherein the disease, disorder or condition is Parkinson's disease.
44. An *in vitro* method of modulating LXR activity comprising contacting LXR, or portion thereof, with a compound according to any one of claims 1-31, or a pharmaceutically acceptable salt thereof.