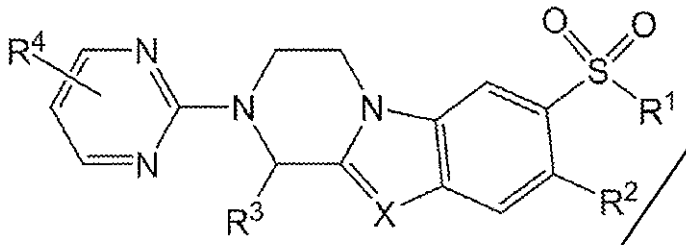
CLAIMS

What is claimed is:

1. A compound represented by the following structural formula:



or a pharmaceutically acceptable salt thereof, wherein:

X is N or CR^c;

R^1 is alkyl or $-NR^aR^b$;

R^2 is H; halogen; -CN; -NRC(O)R; -C(O)OR; $-C(O)NR^aR^b$; monocyclic heteroaromatic optionally substituted with one or more groups selected from alkyl, -CN, -NRC(O)R, -C(O)OR, $-C(O)NR^aR^b$ and halogen; monocyclic non-aromatic heterocycle optionally substituted with one or more groups selected from alkyl, halogen, -CN and =O; or alkyl optionally substituted by one or more groups selected from halogen, hydroxy, alkoxy, $-NR^aR^b$, -NRC(O)R, -NRC(O)O(alkyl), $-NRC(O)N(R)_2$, -C(O)OR, thiol, alkylthiol, nitro, -CN, =O, -OC(O)H, -OC(O)(alkyl), -OC(O)O(alkyl), $-OC(O)N(R)_2$ and $-C(O)NR^aR^b$;

R^3 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, monocyclic non-aromatic heterocycle, monocyclic heteroaromatic or phenyl, wherein the phenyl, monocyclic non-aromatic heterocycle, and monocyclic heteroaromatic group represented by R^3 are optionally substituted with one or more groups selected from alkyl, halogen, haloalkyl, alkoxy, haloalkoxy, nitro and -CN;

R^4 is halogen, -CN, -OR, -SR, $-N(R)_2$, -C(O)R, -C(O)OR, -OC(O)O(alkyl), -C(O)O(haloalkyl), -OC(O)R, $-C(O)N(R)_2$, $-OC(O)N(R)_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, $-SO_2R$, $-SO_2N(R)_2$, -NRS(O)R, $-NRSO_2R$, $-NRC(O)N(R)_2$, $-NRSO_2N(R)_2$, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkyl, monocyclic non-aromatic heterocycle, monocyclic heteroaromatic or alkyl, wherein the monocyclic non-aromatic heterocycle, monocyclic heteroaromatic and alkyl group represented by R^4 are optionally substituted with one or more groups selected from -CN, -OR, -SR, $-N(R)_2$, =O, -C(O)R, -C(O)OR, -C(O)O(haloalkyl),

-OC(O)R, -OC(O)O(alkyl), -C(O)N(R)$_2$, -OC(O)N(R)$_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, -SO$_2$R, -SO$_2$N(R)$_2$, -NRS(O)R, -NRSO$_2$R, -NRC(O)N(R)$_2$ and -NRSO$_2$N(R)$_2$;

Each R independently is H or alkyl;

R^a and R^b are independently H, alkyl or R^a and R^b can be taken together with the nitrogen to which they are attached to form a monocyclic non-aromatic heterocycle; and

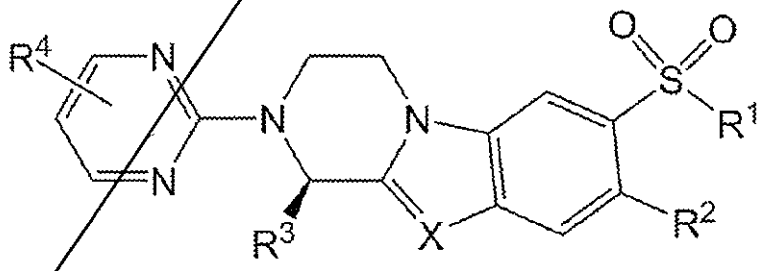
R^c is H, alkyl, or halogen.

2. The compound of claim 1, wherein:

R^3 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl or phenyl, wherein the phenyl represented by R^3 is optionally substituted with one or more groups selected from alkyl, halogen, haloalkyl, alkoxy, haloalkoxy, nitro and -CN;

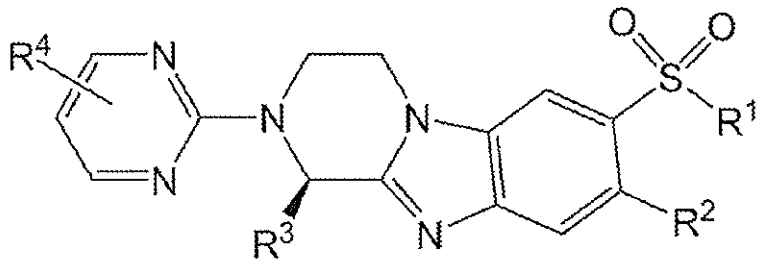
R^4 is halogen, -CN, -OR, -SR, -N(R)$_2$, -C(O)R, -C(O)OR, -OC(O)O(alkyl), -C(O)O(haloalkyl), -OC(O)R, -C(O)N(R)$_2$, -OC(O)N(R)$_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, -SO$_2$R, -SO$_2$N(R)$_2$, -NRS(O)R, -NRSO$_2$R, -NRC(O)N(R)$_2$, -NRSO$_2$N(R)$_2$, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkyl or alkyl, wherein the alkyl group represented by R^4 is optionally substituted with one or more groups selected from –CN, -OR, -SR, -N(R)$_2$, =O, -C(O)R, -C(O)OR, -C(O)O(haloalkyl), -OC(O)R, -OC(O)O(alkyl), -C(O)N(R)$_2$, -OC(O)N(R)$_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, -SO$_2$R, -SO$_2$N(R)$_2$, -NRS(O)R, -NRSO$_2$R, -NRC(O)N(R)$_2$ and –NRSO$_2$N(R)$_2$.

3. The compound of claim 1 or 2, wherein the compound is represented by the following structural formula:



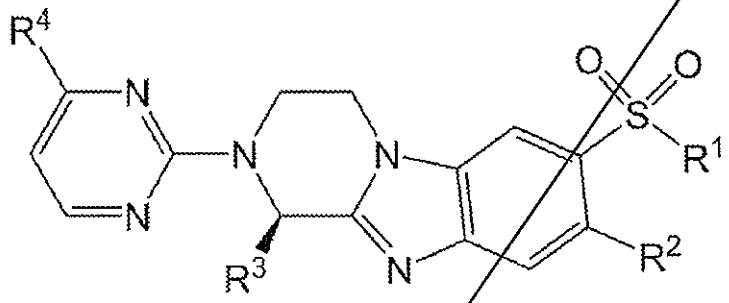
or a pharmaceutically acceptable salt thereof.

4. The compound of claim 1 or 2, wherein the compound is represented by the following structural formula:



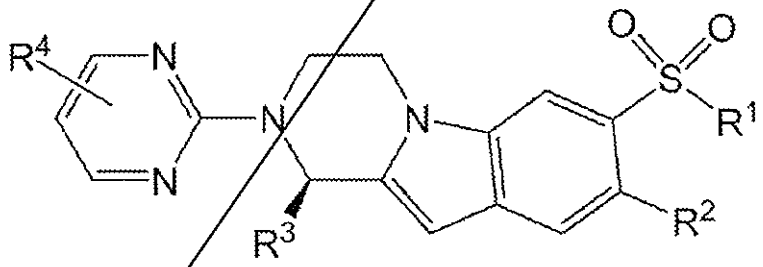
or a pharmaceutically acceptable salt thereof.

5. The compound of claim 4, wherein the compound is represented by the following structural formula:



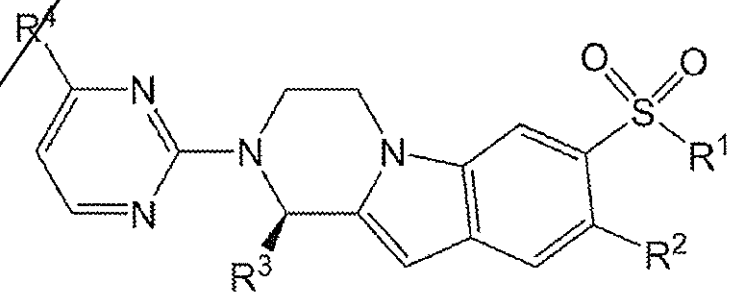
or a pharmaceutically acceptable salt thereof.

6. The compound of claim 1 or 2, wherein the compound is represented by the following structural formula:



or a pharmaceutically acceptable salt thereof.

7. The compound of claim 6, wherein the compound is represented by the following structural formula:



or a pharmaceutically acceptable salt thereof.

8. The compound of any one of the preceding claims, wherein:

R^1 is methyl or $-NH_2$;

R^2 is H or methyl, wherein the methyl group represented by R^2 is optionally substituted with one or more groups selected from halogen, hydroxy, alkoxy, $-NR^aR^b$, -NRC(O)R,

-NRC(O)O(alkyl), $-NRC(O)N(R)_2$, -C(O)OR, thiol, alkylthiol, nitro, -CN, =O, -OC(O)H -OC(O)(alkyl), -OC(O)O(alkyl), $-C(O)NR^aR^b$ and $-OC(O)N(R)_2$;

R^3 is methyl, ethyl, propyl, isopropyl, *tert-butyl*, *sec-butyl*, *iso-butyl*, $-CH_2CF_3$, $-CH(CH_2F)_2$, $-CH(CHF_2)_2$, $-CH(CF_3)_2$, $-CF(CH_3)_2$, $-CF_3$, cyclopropyl, cyclobutyl, cyclopentyl cyclohexyl, $-C(OH)(CH_3)_2$, $-CH(OH)(CH_3)$, or phenyl, wherein the phenyl group represented by R^3 is optionally substituted with one or more groups selected from alkyl, halogen, haloalkyl, alkoxy, haloalkoxy, nitro and -CN; and R^c, where present, is H.

9. The compound of any of the preceding claims, wherein R^2 is H or $-CH_2OH$.

10. The compound of any one of the preceding claims, wherein:

R^1 is methyl;

R^2 is $-CH_2OH$; and R^3 is isopropyl.

11. The compound of any one of the preceding claims, wherein R^4 is halogen, hydroxyl, alkyl, cycloalkyl, cycloalkoxy, alkoxy, haloalkoxy, haloalkyl, $-N(R)_2$, -C(O)OH, -C(O)O(alkyl),

-C(O)O(haloalkyl), -C(O)(alkyl), $-C(O)N(R)_2$, -NRC(O)R, $-SO_2N(R)_2$, $-OC(O)N(R)_2$, -CN, hydroxyalkyl or dihydroxyalkyl.

12. The compound of any one of the preceding claims, wherein R^4 is methyl, ethyl, hydroxyl, CF_3, isopropyl, cyclopropyl, CH_2OH, $-CH(OH)(CH_2)(OH)$, $-C(OH)(CH_3)_2$, $-CH(OH)(CH_3)$,

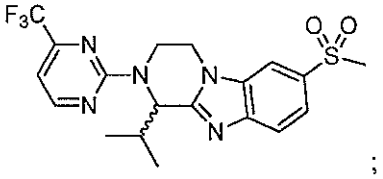
$-CH(OH)(CH_2)(CH_3)$, $-CH(OH)(CH_2)_2(CH_3)$, $-C(O)NH_2$, $C(O)N(CH_3)_2$, -C(O)OH, $-C(O)NH(CH_3)$, $C(O)CH_3$, $C(O)CH_2CH_3$, $C(O)O(CH_2)(CH_3)$, -C(O)O (tert-butyl), $-C(O)O(C)(CH_3)_2(CF_3)$, $-NHC(O)CH_3$, $-OCHF_2$, $-OCF_3$, $-OCH_2CH_3$, $-OCH(CH_3)_2$ or $-OCH_3$.

13. The compound of any one of the preceding claims, wherein R^4 is alkyl, haloalkyl, cycloalkyl, alkoxy, or haloalkoxy.

14. The compound of any one of the preceding claims, wherein R^4 is methyl, halogenated methyl, cyclopropyl, $-OCHF_2$ or $-OCH_3$.

15. The compound of any one of the preceding claims, wherein R^4 is CF_3.

16. A compound represented by a structural formula selected from: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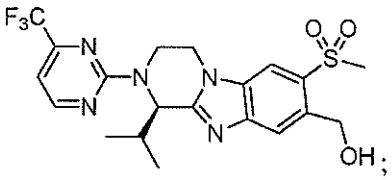
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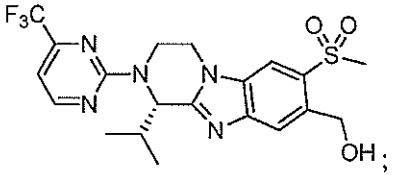
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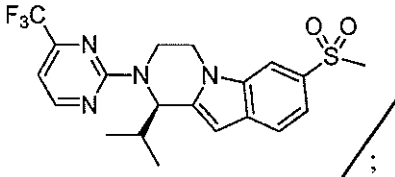
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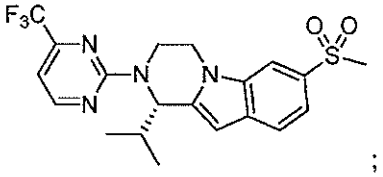
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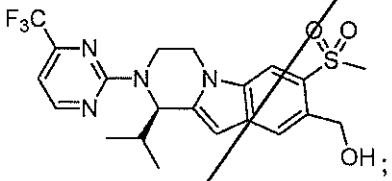
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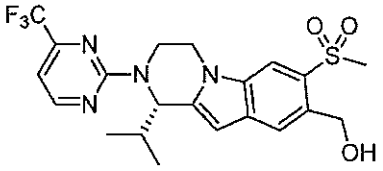

; or a pharmaceutically acceptable salt of any of the foregoing.

17. A pharmaceutical composition comprising a pharmaceutical carrier or diluent and the compound of any one of claims 1-16.

18. A method of treating a subject with a disease or disorder that is treatable by upregulating LXR activity comprising administering an effective amount of the compound of any one of claims 1-16 to the subject.

19. The method of claim 18 wherein the disease or disorder is a lipid disorder; cancer; acneiform skin condition; skin inflammatory disease; immunological disorder; condition characterized by a perturbed epidermal barrier function; condition of disturbed differentiation or excess proliferation of the epidermis or mucous membrane; cardiovascular disease; optic nerve and retinal pathology; degenerative neuropathy occurring in a disease; autoimmune disease; traumatic damage to the central or peripheral nervous system; neurodegenerative disease; a degenerative process due to aging, or diseases or disorders of the kidney.

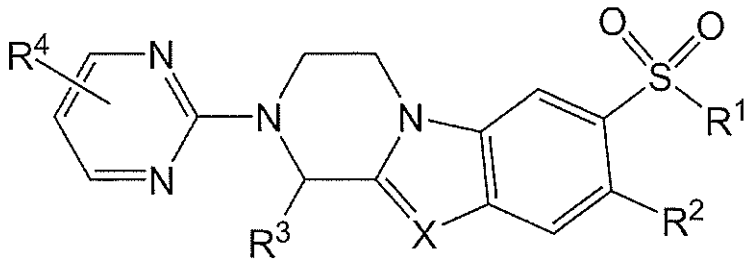
20. The method of claim 19 wherein the disease or disorder is hyperlipidemia, hypercholesterolemia, hyperlipoproteinemia, hypertriglyceridemia, lipodystrophy, hepatic steatosis, nonalcoholic steatohepatitis (NASH), nonalcoholic fatty liver

disease (NAFLD), hyperglycemia, insulin resistance, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, dermatitis, psoriasis, contact dermatitis, atopic dermatitis, eczema, skin wounds, skin aging, photoaging, wrinkling, diabetes, Niemann-Pick disease type C, Parkinson's disease, Alzheimer's disease, inflammation, xanthoma, obesity, metabolic syndrome, syndrome X, stroke, peripheral occlusive disease, memory loss, diabetic neuropathies, proteinuria, glomerulopathies, diabetic nephropathy, hypertensive nephropathy, IGA nephropathy, focal segmental glomerulosclerosis, hyperphosphatemia, cardiovascular complications of hyperphosphatemia, cancer or multiple sclerosis.

21. The method of claim 20 wherein the disease or disorder is atherosclerosis, Alzheimer's disease or dermatitis.

Claims

1. A compound represented by the following structural formula:



or a pharmaceutically acceptable salt thereof, wherein:

X is N or CR^c;

R^1 is alkyl or $-NR^aR^b$;

R^2 is H; halogen; -CN; -NRC(O)R; -C(O)OR; $-C(O)NR^aR^b$; monocyclic heteroaromatic optionally substituted with one or more groups selected from alkyl, -CN, -NRC(O)R, -C(O)OR, $-C(O)NR^aR^b$ and halogen; monocyclic non-aromatic heterocycle optionally substituted with one or more groups selected from alkyl, halogen, -CN and =O; or alkyl optionally substituted by one or more groups selected from halogen, hydroxy, alkoxy, $-NR^aR^b$, -NRC(O)R, -NRC(O)O(alkyl),
$-NRC(O)N(R)_2$, -C(O)OR, thiol, alkylthiol, nitro, -CN, =O, -OC(O)H,
-OC(O)(alkyl), -OC(O)O(alkyl), $-OC(O)N(R)_2$ and $-C(O)NR^aR^b$;

R^3 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, monocyclic non-aromatic heterocycle, monocyclic heteroaromatic or phenyl, wherein the phenyl, monocyclic non-aromatic heterocycle, and monocyclic heteroaromatic group represented by R^3 are optionally substituted with one or more groups selected from alkyl, halogen, haloalkyl, alkoxy, haloalkoxy, nitro and -CN;

R^4 is halogen, -CN, -OR, -SR, $-N(R)_2$, -C(O)R, -C(O)OR, -OC(O)O(alkyl),
-C(O)O(haloalkyl), -OC(O)R, $-C(O)N(R)_2$, $-OC(O)N(R)_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, $-SO_2R$, $-SO_2N(R)_2$, -NRS(O)R, $-NRSO_2R$, $-NRC(O)N(R)_2$, $-NRSO_2N(R)_2$, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkyl, monocyclic non-aromatic heterocycle, monocyclic heteroaromatic or alkyl, wherein the monocyclic non-aromatic heterocycle, monocyclic heteroaromatic and alkyl group represented by R^4 are optionally substituted with one or more groups selected from -CN, -OR, -SR, $-N(R)_2$, =O, -C(O)R, -C(O)OR, -C(O)O(haloalkyl), -OC(O)R, -OC(O)O(alkyl), $-C(O)N(R)_2$, $-OC(O)N(R)_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, $-SO_2R$, $-SO_2N(R)_2$, -NRS(O)R, $-NRSO_2R$, $-NRC(O)N(R)_2$ and $-NRSO_2N(R)_2$;

Each R independently is H or alkyl;

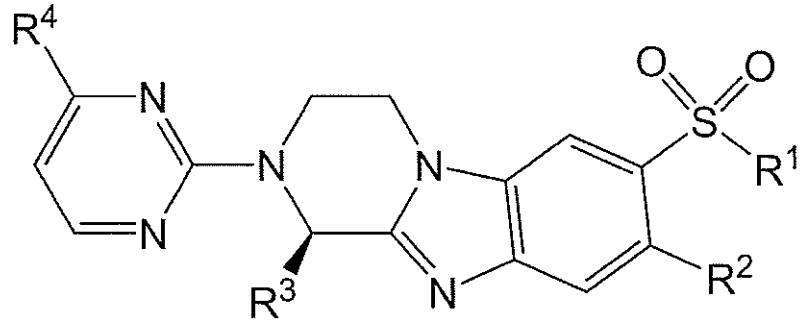
R^a and R^b are independently H, alkyl or R^a and R^b can be taken together with the nitrogen to which they are attached to form a monocyclic non-aromatic heterocycle; and R^c is H, alkyl, or halogen.

2. The compound of claim 1, wherein:

R^3 is alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl or phenyl, wherein the phenyl represented by R^3 is optionally substituted with one or more groups selected from alkyl, halogen, haloalkyl, alkoxy, haloalkoxy, nitro and -CN;

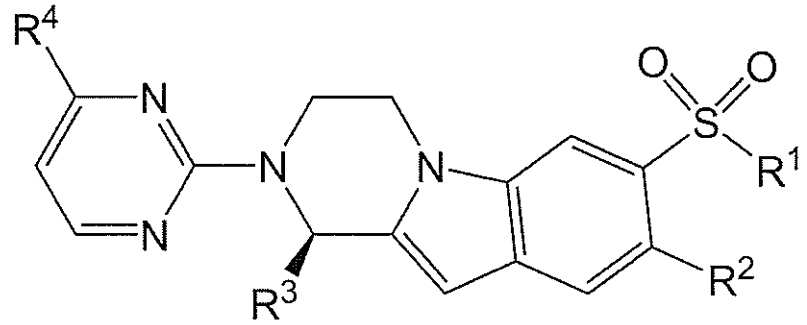
R^4 is halogen, -CN, -OR, -SR, $-N(R)_2$, -C(O)R, -C(O)OR, -OC(O)O(alkyl), -C(O)O(haloalkyl), -OC(O)R, $-C(O)N(R)_2$, $-OC(O)N(R)_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, $-SO_2R$, $-SO_2N(R)_2$, -NRS(O)R, $-NRSO_2R$, $-NRC(O)N(R)_2$, $-NRSO_2N(R)_2$, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkyl or alkyl, wherein the alkyl group represented by R^4 is optionally substituted with one or more groups selected from –CN, -OR, -SR, $-N(R)_2$, =O, -C(O)R, -C(O)OR, -C(O)O(haloalkyl), -OC(O)R, -OC(O)O(alkyl), $-C(O)N(R)_2$, $-OC(O)N(R)_2$, -NRC(O)R, -NRC(O)O(alkyl), -S(O)R, $-SO_2R$, $-SO_2N(R)_2$, -NRS(O)R, $-NRSO_2R$, $-NRC(O)N(R)_2$ and $-NRSO_2N(R)_2$.

3. The compound of claim 1 or 2, wherein the compound is represented by the following structural formula:



or a pharmaceutically acceptable salt thereof.

4. The compound of claim 1 or 2, wherein the compound is represented by the following structural formula:



or a pharmaceutically acceptable salt thereof.

5. The compound of any one of the preceding claims, wherein:
R^1 is methyl or $-NH_2$;
R^2 is H or methyl, wherein the methyl group represented by R^2 is optionally substituted with one or more groups selected from halogen, hydroxy, alkoxy, $-NR^aR^b$, -NRC(O)R, -NRC(O)O(alkyl), $-NRC(O)N(R)_2$, -C(O)OR, thiol, alkylthiol, nitro, -CN, =O, -OC(O)H -OC(O)(alkyl), -OC(O)O(alkyl), $-C(O)NR^aR^b$ and $-OC(O)N(R)_2$;
R^3 is methyl, ethyl, propyl, isopropyl, tert-butyl, sec-butyl, iso-butyl, $-CH_2CF_3$, $-CH(CH_2F)_2$, $-CH(CHF_2)_2$, $-CH(CF_3)_2$, $-CF(CH_3)_2$, $-CF_3$, cyclopropyl, cyclobutyl, cyclopentyl cyclohexyl, $-C(OH)(CH_3)_2$, $-CH(OH)(CH_3)$, or phenyl, wherein the phenyl group represented by R^3 is optionally substituted with one or more groups selected from alkyl, halogen, haloalkyl, alkoxy, haloalkoxy, nitro and -CN; and R^c, where present, is H.

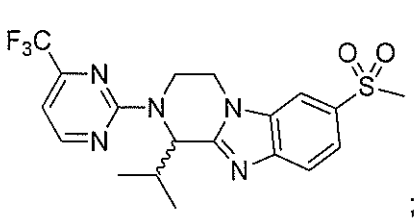
6. The compound of any one of the preceding claims, wherein:
R^1 is methyl;
R^2 is $-CH_2OH$;
R^3 is isopropyl; and
R^4 is halogen, hydroxy, alkyl, cycloalkyl, cycloalkoxy, alkoxy, haloalkoxy, haloalkyl, $-N(R)_2$, -C(O)OH, -C(O)O(alkyl), -C(O)O(haloalkyl), -C(O)(alkyl), $-C(O)N(R)_2$, -NRC(O)R, $-SO_2N(R)_2$, $-OC(O)N(R)_2$, -CN, hydroxyalkyl or dihydroxyalkyl.

7. The compound of any one of the preceding claims, wherein R^4 is methyl, ethyl, hydroxy, CF_3, isopropyl, cyclopropyl, CH_2OH, $-CH(OH)(CH_2)(OH)$, $-C(OH)(CH_3)_2$, $-CH(OH)(CH_3)$, $-CH(OH)(CH_2)(CH_3)$, $-CH(OH)(CH_2)_2(CH_3)$, $-C(O)NH_2$, $C(O)N(CH_3)_2$, -C(O)OH, $-C(O)NH(CH_3)$, $C(O)CH_3$, $C(O)CH_2CH_3$, $C(O)O(CH_2)(CH_3)$, -C(O)O (tert-butyl), $-C(O)O(C)(CH_3)_2(CF_3)$, $-NHC(O)CH_3$, $-OCHF_2$, $-OCF_3$, $-OCH_2CH_3$, $-OCH(CH_3)_2$ or $-OCH_3$.

8. The compound of any one of the preceding claims, wherein R^4 is methyl, CF_3, cyclopropyl, $-OCHF_2$ or $-OCH_3$.

9. The compound of any one of the preceding claims, wherein R^4 is CF_3.

10. The compound of claim 1, wherein the compound is represented by a structural formula selected from: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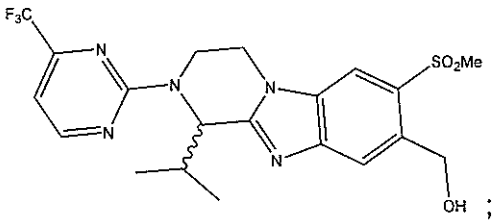
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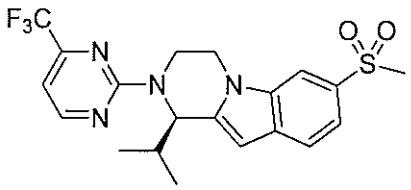
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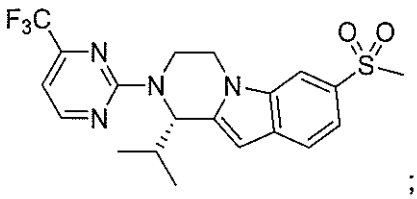
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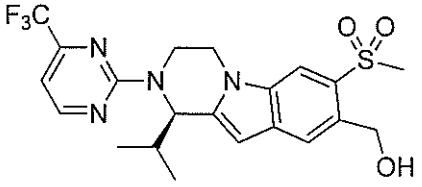
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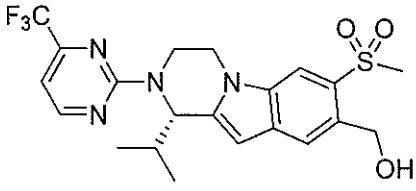
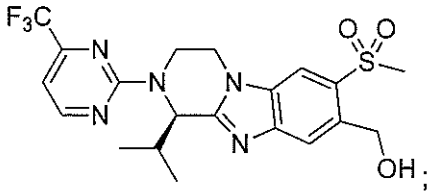

; or a pharmaceutically acceptable salt of any of the foregoing.

11. The compound of claim 10, wherein the compound is represented by the following structural formula:


;

or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition comprising a pharmaceutical carrier or diluent and the compound of any one of claims 1 to 11.