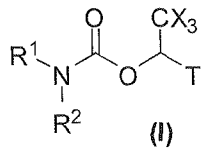
[0006] The serine hydrolase α–β-hydrolase domain 6 (ABHD6) is another lipid mediator and also may control accumulation and efficacy of 2-AG at cannabinoid receptors. ABHD6 may be a rate-limiting step of 2-AG signaling and thus is a member of the endocannabinoid signaling system. Therefore, ABHD6 may also be a useful target for cannabinoid dependent disorders, alone or in conjunction with MAGL and/or another serine hydrolase.

SUMMARY

[0007] This disclosure provides, for example, compounds and compositions which may be modulators of MAGL and/or ABHD6, and their use as medicinal agents, processes for their preparation, and pharmaceutical compositions that include disclosed compounds as at least one active ingredient. The disclosure also provided for the use of disclosed compounds as medicaments and/or in the manufacture of medicaments for the inhibition of MAGL and/or ABHD6 activity in warm-blooded animals such as humans.

[0008] In an embodiment, provided herein are compounds represented by formula I:

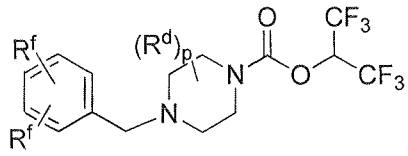
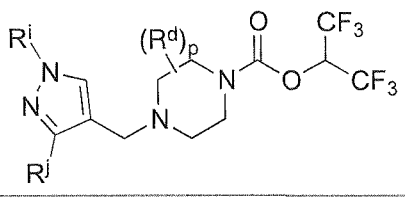


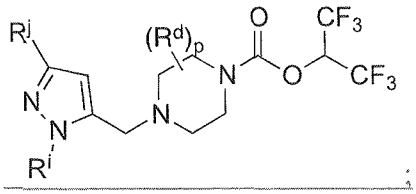
(I)

or pharmaceutically acceptable salts, stereoisomers, esters or prodrugs thereof, where R^1, R^2, T, and X are as defined herein.

[0009] The disclosure also provides for methods of treating indications such as pain, solid tumor cancer, or obesity via administration of a disclosed compound. Also provided are pharmaceutical compositions comprising at least one disclosed compound and a pharmaceutically acceptable carrier.

[0009a] In one aspect, there is provided a compound represented by:



, and


;

wherein

R^f is independently selected for each occurrence from H, R^aR^bN-, R^aR^bN-C(O)-, phenyoxy, halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens) and C_{1-6}alkoxy (optionally substituted by one, two or three halogens) wherein R^a and R^b together with the nitrogen to which they are attached, form a 4-6 membered heterocyclic ring or a 9-10 membered bicyclic heterocyclic ring or spirocycle, which may have an additional heteroatom selected from O, S, and N; wherein the 4-6 membered heterocyclic ring or 9-10 membered bicyclic heterocyclic ring or spirocycle may optionally be substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, hydroxyl, -NH_2, -$S(O)_w$- C_{1-6}alkyl (wherein w is 0, 1 or 2) and NH-C(O)-C_{1-6}alkyl;

R^i and R^j may be independently selected from the group consisting of: H, CH_3, C_{2-6}alkyl (optionally substituted by one, two or three moieties independently selected from R^c)), phenyl (optionally substituted by one, two or three moieties independently selected from R^c), and C_{3-6}cycloalkyl (optionally substituted by one, two or three moieties independently selected from R^c);

R^a and R^b, when they occur together with the nitrogen to which they are attached, form a 4-6 membered heterocyclic ring or a 9-10 membered bicyclic heterocycle or spirocyclic ring, which may have an additional heteroatom selected from O, S, or N; wherein the 4-6 membered heterocyclic ring or 9-10 membered bicyclic heterocycle or spirocycle may optionally be substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl;

R^c is selected from the group consisting of halogen, cyano, hydroxyl, nitro, C_{1-6}alkyl (optionally substituted by one, two, or three halogens, cyano, or hydroxyl), C_{2-6}alkenyl (optionally substituted by one, two, or three halogens), C_{2-6}alkynyl (optionally substituted by one, two, or three halogens), C_{3-6}cycloalkyl, C_{1-6}alkoxy (optionally substituted by one, two, or three halogens), R^aR^bN-, R^aR^bN-SO_2-, R^aR^bN-C(O)-, R^a-C(O)-NR^a-, R^a-C(O)-, R^a-$S(O)_w$-NR^b- (wherein w is 0, 1 or 2), or R^a-$S(O)_w$- (wherein w is 0, 1 or 2);

p is 0, 1, or 2; and

R^d is $-CH_3$;

or a pharmaceutically acceptable salt or stereoisomer thereof.

[0009b] In one aspect, there is provided a compound wherein the compound is 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate; or a pharmaceutically acceptable salt thereof.

[0009c] In one aspect, there is provided a compound selected from the group consisting of:

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[bis(4-chlorophenyl)methyl]-3-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(oxazol-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(4-chloro-2-methylphenyl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(1-methyl-1*H*-indazol-5-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(di(pyridin-3-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-fluoro-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-phenoxybenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-(morpholin-4-yl)-3-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-fluoro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-chloro-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-4-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-4-[[2-fluoro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-2-methyl-4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-4-[[2-fluoro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-2-methyl-4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-6-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-chloro-2-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chlorobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methyl-4-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-(piperidin-1-yl)benzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methoxy-4-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methyl-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-methoxybenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-methylbenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-4-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-6-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-chloro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-chloro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(4-chloro-1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(trifluoromethoxy)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-4-[[2-chloro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-4-[[2-chloro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

(S)-1,1,1,3,3,3-hexafluoropropan-2-yl 2-methyl-4-(4-morpholino-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 2-methyl-4-(4-morpholino-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(pyrrolidin-1-yl)-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-isopropyl-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-isopropyl-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(8-oxa-2-azaspiro[4.5]decan-2-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(4-acetylpiperazin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(1-oxo-2,8-diazaspiro[4.5]decan-8-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(azetidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-4-(1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

(*S*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(propan-2-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-chloro-4-(pyrrolidine-1-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(azetidine-1-carbonyl)-2-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(morpholine-4-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(pyrrolidine-1-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(5*H*-pyrrolo[3,4-*b*]pyridin-6(7*H*)-yl)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(4-(methylsulfonyl)piperazin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((5-(4-methoxyphenyl)isoxazol-3-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((5-phenylisoxazol-3-yl)methyl)piperazine-1-carboxylate,

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-methyl-1-phenyl-1H-pyrazol-4-yl)methyl)piperazine-1-carboxylate,

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((1-methyl-3-phenyl-1H-pyrazol-5-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((1-methyl-3-phenyl-1H-pyrazol-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((4-bromo-1-methyl-1*H*-pyrazol-5-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-(2-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-phenyl-1-(propan-2-yl)-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-(2-chlorophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 3-methyl-4-[(4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-6-(2-methylphenyl)pyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-(2-fluorophenyl)-2-methylpyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-6-(3-methylphenyl)pyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-(3-fluorophenyl)-2-methylpyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-morpholino-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(2-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(3-methylphenyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(2-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-methoxy-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(pyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(2,6-dimethylpyridin-4-yl)-2-methylphenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(3-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(3-fluorophenyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-fluoro-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-methyl-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(3-methylphenyl)-2-phenoxyphenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(2-methylpyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(2-methylpyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-methyl-5-(2-methylphenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)-6-methylpyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-(dimethylcarbamoyl)-4-phenylphenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-([4-phenyl-2-[(pyrrolidin-1-yl)carbonyl]phenyl]methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(6-methylpyridin-2-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(2,6-dimethylpyridin-4-yl)-2-fluorophenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(3-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(6-methylpyridin-2-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-methyl-5-(3-methylphenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate
or a pharmaceutically acceptable salt or stereoisomer thereof.

[0009d] In one aspect, there is provided a pharmaceutically acceptable composition comprising a compound as described herein, and a pharmaceutically acceptable excipient.

[0009e] In one aspect, there is provided the use of a compound as described herein in the manufacture of a medicament for the treatment of pain.

[0009f] In one aspect, there is provided the use of a compound as described herein in the manufacture of a medicament for the treatment of solid tumor cancer.

[0009g] In one aspect, there is provided the use of a compound as described herein in the manufacture of a medicament for the treatment of Downs syndrome or Alzheimer's disease.

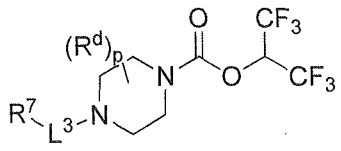
DETAILED DESCRIPTION

[0010] This disclosure is directed, at least in part, to MAGL and/or ABHD6 modulators or inhibitors. For example, provided herein are compounds capable of inhibiting MAGL and/or ABHD6.

[0011] The features and other details of the disclosure will now be more particularly described. Before further description, certain terms employed in the specification, examples

What is claimed is:

1. A compound represented by:



wherein

L^3 is selected from the group consisting of: C_1-C_6alkylene, -C(O)-, C_1-C_6alkylene-C(O)-, C(O)-C_1-C_6alkylene-, NR^a-C(O)-C_1-C_6alkylene-, C_1-C_6alkylene-O-C(O)-, -$S(O)_w$-, and C_1-C_6alkylene-$S(O)_w$-, wherein w is 0, 1, or 2, and wherein C_1-C_6alkylene is optionally substituted by one or two substituents selected from the group consisting of: halogen, hydroxyl, cyano, and an additional R^7, wherein when L^3 is -$S(O)_w$-, then R^7 is not H;

R^7 is selected from the group consisting of: H, phenyl, naphthyl, mono or bicyclic heteroaryl, and mono or bicyclic heterocyclyl, wherein the heteroaryl or the heterocyclyl has 1, 2 or 3 heteroatoms independently selected from O, S, or N; wherein R^7 is optionally substituted by one, two, three or four moieties independently selected from R^h;

R^a and R^b are independently selected, for each occurrence, from the group consisting of hydrogen and C_{1-3}alkyl; wherein C_{1-3}alkyl may optionally be substituted by one or more substituents selected from halogen, cyano, oxo, hydroxyl, heterocycle, and phenyl;

or R^a and R^b, when they occur together with the nitrogen to which they are attached, form a 4-6 membered heterocyclic ring or a 9-10 membered bicyclic heterocycle or spirocyclic ring, which may have an additional heteroatom selected from O, S, or N; wherein the 4-6 membered heterocyclic ring or 9-10 membered bicyclic heterocycle or spirocycle may optionally be substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl;

R^h is selected from the group consisting of: halogen, phenyl (optionally substituted by one, two, or three moieties each independently selected from R^c), phenyloxy (optionally substituted by one, two, or three moieties each independently selected from R^c), hydroxyl, cyano, C_{1-6}alkyl (optionally substituted by one, two or three halogens, cyano, or hydroxyl), C_{2-6}alkenyl (optionally substituted by one, two or three halogens, cyano, or hydroxyl), C_{2-}

$_{6}$alkynyl (optionally substituted by one, two or three halogens, cyano, or hydroxyl), C_{1-6}alkoxy (optionally substituted by one, two or three halogens, cyano, or hydroxyl), R^aR^bN-, R^a-C(O)NR^a-, R^aR^bN-SO_2-, R^aR^bN-C(O)-, R^a-$S(O)_w$- (wherein w is 0, 1 or 2), R^a-SO_2-NR^b-, heteroaryl (optionally substituted by one, two or three moieties each independently selected from R^c, and connected to R^7 through a carbon or heteroatom), heterocycle (optionally substituted by one, two or three moieties each independently selected from R^c, and connected to R^7 through a carbon or heteroatom) or heteroaryloxy (optionally substituted by one, two, or three moieties each independently selected from R^c), or two adjacent R^h groups along with the carbons to which they are attached can be taken together to form a 5- or 6- member heterocyclic or heteroaryl ring optionally substituted with 0, 1 or 2 halogens selected from F or Cl and which may have one or two additional heteroatoms selected from O, S, or N;

p is 0, 1, or 2; and

R^d is selected from the group consisting of: H, C_{1-6}alkyl (optionally substituted by one, two or three halogens, or hydroxyl) or R^aR^bN-C(O)-;

or a pharmaceutically acceptable salts or stereoisomers thereof.

2. The compound of claim 1, wherein:

L^3 is selected from the group consisting of C_1-C_2alkylene, -C(O)-, -CH-C(O)-NH, -$S(O)_w$-, and C_1-C_2alkylene-$S(O)_w$-, wherein w is 0, 1, or 2, and wherein C_1-C_2alkylene is optionally substituted by a substituent selected from the group consisting of: phenyl, biphenyl, phenyloxyphenyl (each optionally substituted by halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens, or hydroxyl)), mono or bicyclic heteroaryl having 1, 2 or 3 heteroatoms independently selected from O, S, or N and mono or bicyclic heterocycle having 1, 2 or 3 heteroatoms independently selected from O, S, or N; and

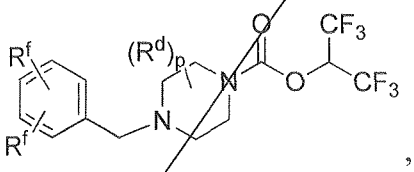
R^7 is selected from the group consisting of phenyl, biphenyl, phenyloxyphenyl, and mono or bicyclic heteroaryl or mono or bicyclic heterocycle, wherein the heteroaryl or heterocycle has 1, 2 or 3 heteroatoms independently selected from O, S, or N, and R^7 is optionally substituted by one, two, three or four substituents selected from the group consisting of halogen, cyano, phenyl (optionally substituted by one, two, or three substituents selected from the group consisting of: halogen, methyl, ethyl, propyl, t-butyl, cyano or CF_3), phenyloxy, hydroxyl, cyano, C_{1-6}alkyl (optionally substituted by one, two or three halogens, or hydroxyl), C_{1-}

$_{6}$alkoxy (optionally substituted by one, two or three halogens), R^aR^bN-, R^aR^bN-SO_2-, R^a-$S(O)_w$-NR^b- (wherein w is 0, 1 or 2), R^aR^bN-C(O)-, C_{1-6}alkyl-$C(O)NR^a$-, heteroaryl (optionally substituted by one or two substituents each selected from C_{1-6}alkyl or halogen), or heteroaryloxy (optionally substituted by one or two substituents each selected from C_{1-6}alkyl or halogen).

3. The compound of claim 1 or 2, wherein L^3 is selected from the group consisting of -CH_2-, -$S(O)_2$-, or –C(O)-.

4. The compound of claim 1 or 2, wherein R^7 is selected from the group consisting of phenyl, naphthyl, indanyl, benzodioxole, benzoxazole, benzoisoxazole, benzimidazole, benzotriazole, oxadiazole, indazole, isooxazole, quinoline, isoquinoline, pyridine, pyrazine, pyrimidine, thienyl, thiazole, benzothiopene, indole, benzothiadiazole, pyrazole, or 3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine, and R^7 is optionally substituted by one, two, three or four substituents selected from the group consisting of halogen, phenyl (optionally substituted by one, two, or three substituents selected from the group consisting of: halogen, methyl, ethyl, propyl, t-butyl, cyano or CF_3), phenyloxy, hydroxyl, cyano, C_{1-6}alkyl (optionally substituted by one, two or three halogens, or hydroxyl), C_{1-6}alkoxy(optionally substituted by one, two or three halogens), R^aR^bN-, R^aR^bN-SO_2-, R^a-$S(O)_w$-NR^b- (wherein w is 0, 1 or 2), R^aR^bN-C(O)-, C_{1-6}alkyl-$C(O)NR^a$-, heteroaryl (optionally substituted by one or two substituents each selected from C_{1-6}alkyl or halogen), or heteroaryloxy.

5. The compound of any one of claims 1-4, represented by a formula selected from the group consisting of:



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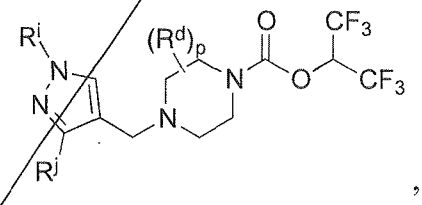
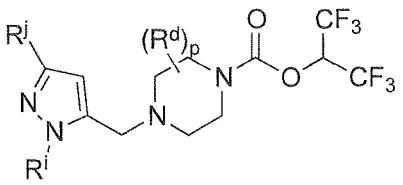




, and

wherein R^f is independently selected for each occurrence from H, R^aR^bN-, R^aR^bN-C(O)-, phenyoxy, halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens) and C_{1-6}alkoxy (optionally substituted by one, two or three halogens) wherein R^a and R^b together with the nitrogen to which they are attached, form a 4-6 membered heterocyclic ring or a 9-10 membered bicyclic heterocyclic ring or spirocycle, which may have an additional heteroatom selected from O, S, or N; wherein the 4-6 membered heterocyclic ring or 9-10 membered bicyclic heterocyclic ring or spirocycle may optionally be substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, hydroxyl, $-NH_2$, $-S(O)_w-$ C_{1-6}alkyl (wherein w is 0, 1 or 2) and NH-C(O)-C_{1-6}alkyl.

6. The compound of claim 5, wherein one R_f is a heterocyclic ring selected from piperidinyl, pyrrolidinyl, morpholinyl, and pyrazole.

7. A compound selected from the group consisting of:
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[bis(4-chlorophenyl)methyl]-3-methylpiperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(oxazol-4-yl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(4-chloro-2-methylphenyl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(1-methyl-1*H*-indazol-5-yl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(di(pyridin-3-yl)methyl)piperazine-1-carboxylate
1,1,1-trifluoro-3-methoxy-3-oxopropan-2-yl 4-(bis(4-chlorophenyl)methyl)piperazine-1-carboxylate
2-((4-(bis(4-chlorophenyl)methyl)piperazine-1-carbonyl)oxy)-3,3,3-trifluoropropanoic acid
1,1,1-trifluoro-3-(methylamino)-3-oxopropan-2-yl 4-(bis(4-chlorophenyl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-fluoro-4-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-phenoxybenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-(morpholin-4-yl)-3-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-fluoro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-chloro-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-4-[[2-fluoro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-2-methyl-4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-4-[[2-fluoro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-2-methyl-4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-6-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-chloro-2-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methyl-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-(piperidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methoxy-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methyl-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-methoxybenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-methylbenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-4-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-6-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-chloro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-chloro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(4-chloro-1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(trifluoromethoxy)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-4-[[2-chloro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-4-[[2-chloro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

(S)-1,1,1,3,3,3-hexafluoropropan-2-yl 2-methyl-4-(4-morpholino-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 2-methyl-4-(4-morpholino-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(pyrrolidin-1-yl)-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-isopropyl-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-isopropyl-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(8-oxa-2-azaspiro[4.5]decan-2-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(4-acetylpiperazin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(1-oxo-2,8-diazaspiro[4.5]decan-8-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(azetidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-4-(1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

(*S*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(propan-2-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-chloro-4-(pyrrolidine-1-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(azetidine-1-carbonyl)-2-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(morpholine-4-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(pyrrolidine-1-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(5*H*-pyrrolo[3,4-*b*]pyridin-6(7*H*)-yl)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(4-(methylsulfonyl)piperazin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((5-(4-methoxyphenyl)isoxazol-3-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((5-phenylisoxazol-3-yl)methyl)piperazine-1-carboxylate,

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-methyl-1-phenyl-1H-pyrazol-4-yl)methyl)piperazine-1-carboxylate,

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((1-methyl-3-phenyl-1H-pyrazol-5-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((1-methyl-3-phenyl-1H-pyrazol-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((4-bromo-1-methyl-1*H*-pyrazol-5-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-(2-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-phenyl-1-(propan-2-yl)-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-(2-chlorophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 3-methyl-4-[(4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-6-(2-methylphenyl)pyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-(2-fluorophenyl)-2-methylpyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-6-(3-methylphenyl)pyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-(3-fluorophenyl)-2-methylpyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-morpholino-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(2-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(3-methylphenyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(2-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-methoxy-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(pyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(2,6-dimethylpyridin-4-yl)-2-methylphenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(3-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(3-fluorophenyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-fluoro-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-methyl-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(3-methylphenyl)-2-phenoxyphenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(2-methylpyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(2-methylpyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-methyl-5-(2-methylphenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)-6-methylpyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-(dimethylcarbamoyl)-4-phenylphenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-([4-phenyl-2-[(pyrrolidin-1-yl)carbonyl]phenyl]methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(6-methylpyridin-2-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(2,6-dimethylpyridin-4-yl)-2-fluorophenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(3-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(6-methylpyridin-2-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-methyl-5-(3-methylphenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate
or a pharmaceutically acceptable salt or stereoisomer thereof.

8. A pharmaceutically acceptable composition comprising a compound of any one of claims 1-7, and a pharmaceutically acceptable excipient.

9. Use of a compound of any one of claims 1-7 in the manufacture of a medicament for the treatment of pain.

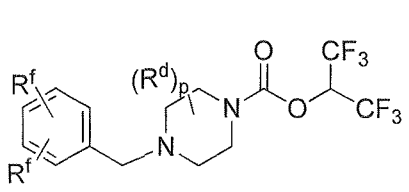
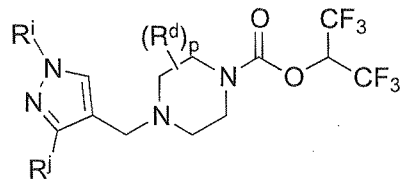
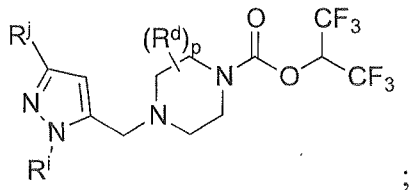
10. Use of a compound of any one of claims 1-7 in the manufacture of a medicament for the treatment of solid tumor cancer.

11. Use of a compound of any one of claims 1-7 in the manufacture of a medicament for the treatment of obesity or reduction of adipose tissue.

12. Use of a compound of any one of claims 1-7 in the manufacture of a medicament for the treatment of Downs syndrome or Alzheimer's disease.

What is claimed is

1. A compound represented by:


,

, and

;

wherein

R^f is independently selected for each occurrence from H, R^aR^bN-, R^aR^bN-C(O)-, phenyoxy, halogen, C_{1-6}alkyl (optionally substituted by one, two or three halogens) and C_{1-6}alkoxy (optionally substituted by one, two or three halogens) wherein R^a and R^b together with the nitrogen to which they are attached, form a 4-6 membered heterocyclic ring or a 9-10 membered bicyclic heterocyclic ring or spirocycle, which may have an additional heteroatom selected from O, S, and N; wherein the 4-6 membered heterocyclic ring or 9-10 membered bicyclic heterocyclic ring or spirocycle may optionally be substituted by one or more substituents selected from the group consisting of halogen, cyano, oxo, C_{1-6}alkyl, hydroxyl, -NH_2, -$S(O)_w$- C_{1-6}alkyl (wherein w is 0, 1 or 2) and NH-C(O)-C_{1-6}alkyl;

R^i and R^j may be independently selected from the group consisting of: H, CH_3, C_{2-6}alkyl (optionally substituted by one, two or three moieties independently selected from R^c)), phenyl (optionally substituted by one, two or three moieties independently selected from R^c), and C_{3-6}cycloalkyl (optionally substituted by one, two or three moieties independently selected from R^c);

R^a and R^b, when they occur together with the nitrogen to which they are attached, form a 4-6 membered heterocyclic ring or a 9-10 membered bicyclic heterocycle or spirocyclic ring, which may have an additional heteroatom selected from O, S, or N; wherein the 4-6 membered heterocyclic ring or 9-10 membered bicyclic heterocycle or spirocycle may optionally be substituted by one or more substituents selected from the group consisting of

halogen, cyano, oxo, C_{1-6}alkyl, -$S(O)_w$-C_{1-6}alkyl (where w is 0, 1 or 2), hydroxyl, -C(O)-C_{1-6}alkyl, -NH_2, and -NH-C(O)-C_{1-6}alkyl;

R^c is selected from the group consisting of halogen, cyano, hydroxyl, nitro, C_{1-6}alkyl (optionally substituted by one, two, or three halogens, cyano, or hydroxyl), C_{2-6}alkenyl (optionally substituted by one, two, or three halogens), C_{2-6}alkynyl (optionally substituted by one, two, or three halogens), C_{3-6}cycloalkyl, C_{1-6}alkoxy (optionally substituted by one, two, or three halogens), R^aR^bN-, R^aR^bN-SO_2-, R^aR^bN-C(O)-, R^a-C(O)-NR^a-, R^a-C(O)-, R^a-$S(O)_w$-NR^b- (wherein w is 0, 1 or 2), or R^a-$S(O)_w$- (wherein w is 0, 1 or 2);

p is 0, 1, or 2; and

R^d is -CH_3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. The compound of claim 1, wherein one R_f is a heterocyclic ring selected from piperidinyl, pyrrolidinyl, morpholinyl, and pyrazole.

3. A compound wherein the compound is 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate; or a pharmaceutically acceptable salt thereof.

4. A compound selected from the group consisting of:
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[bis(4-chlorophenyl)methyl]-3-methylpiperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(oxazol-4-yl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(4-chloro-2-methylphenyl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(1-methyl-1*H*-indazol-5-yl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(di(pyridin-3-yl)methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-fluoro-4-morpholinobenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-phenoxybenzyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-(morpholin-4-yl)-3-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-fluoro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-chloro-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-4-[[2-fluoro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-2-methyl-4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-4-[[2-fluoro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-2-methyl-4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-6-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-chloro-2-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methyl-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-(piperidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methoxy-4-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-methyl-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-methoxybenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-methylbenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-bromo-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-4-(pyrrolidin-1-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-chloro-6-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-chloro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-chloro-2-(morpholin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-morpholinobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(4-chloro-1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(trifluoromethyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(trifluoromethoxy)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2S)-4-[[2-chloro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl (2R)-4-[[2-chloro-4-(morpholin-4-yl)phenyl]methyl]-2-methylpiperazine-1-carboxylate

(S)-1,1,1,3,3,3-hexafluoropropan-2-yl 2-methyl-4-(4-morpholino-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 2-methyl-4-(4-morpholino-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(pyrrolidin-1-yl)-2-(trifluoromethoxy)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-2-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-isopropyl-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-isopropyl-4-(pyrrolidin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(8-oxa-2-azaspiro[4.5]decan-2-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(4-acetylpiperazin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(1-oxo-2,8-diazaspiro[4.5]decan-8-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(azetidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-fluoro-4-(1*H*-pyrazol-1-yl)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

(*S*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(3-acetamidopyrrolidin-1-yl)-4-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(morpholin-4-yl)-2-(propan-2-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-chloro-4-(pyrrolidine-1-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-(azetidine-1-carbonyl)-2-chlorobenzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(morpholine-4-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(3-chloro-2-(pyrrolidine-1-carbonyl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(5*H*-pyrrolo[3,4-*b*]pyridin-6(7*H*)-yl)benzyl)piperazine-1-carboxylate

(*R*)-1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-(4-chloro-2-(4-(methylsulfonyl)piperazin-1-yl)benzyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((5-(4-methoxyphenyl)isoxazol-3-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((5-phenylisoxazol-3-yl)methyl)piperazine-1-carboxylate,

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-methyl-1-phenyl-1H-pyrazol-4-yl)methyl)piperazine-1-carboxylate,

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((1-methyl-3-phenyl-1H-pyrazol-5-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((1-methyl-3-phenyl-1H-pyrazol-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((4-bromo-1-methyl-1*H*-pyrazol-5-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-(2-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-phenyl-1-(propan-2-yl)-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[3-(2-chlorophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 3-methyl-4-[(4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-6-(2-methylphenyl)pyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-(2-fluorophenyl)-2-methylpyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-6-(3-methylphenyl)pyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-(3-fluorophenyl)-2-methylpyridin-3-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-((3-morpholino-[1,1'-biphenyl]-4-yl)methyl)piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(2-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(3-methylphenyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(2-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-methoxy-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(pyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(2,6-dimethylpyridin-4-yl)-2-methylphenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(3-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(3-fluorophenyl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-fluoro-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[(2-methyl-4-phenylphenyl)methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(3-methylphenyl)-2-phenoxyphenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(2-methylpyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(2-methylpyridin-3-yl)phenyl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-methyl-5-(2-methylphenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate

1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[5-(3-fluorophenyl)-6-methylpyridin-2-yl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-(dimethylcarbamoyl)-4-phenylphenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-([4-phenyl-2-[(pyrrolidin-1-yl)carbonyl]phenyl]methyl)piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-methyl-4-(6-methylpyridin-2-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[4-(2,6-dimethylpyridin-4-yl)-2-fluorophenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(3-methylpyridin-4-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[2-fluoro-4-(6-methylpyridin-2-yl)phenyl]methyl]piperazine-1-carboxylate
1,1,1,3,3,3-hexafluoropropan-2-yl 4-[[6-methyl-5-(3-methylphenyl)pyridin-2-yl]methyl]piperazine-1-carboxylate
or a pharmaceutically acceptable salt or stereoisomer thereof.

5. A pharmaceutically acceptable composition comprising a compound of any one of claims 1-4, and a pharmaceutically acceptable excipient.

6. Use of a compound of any one of claims 1-4 in the manufacture of a medicament for the treatment of pain.

7. Use of a compound of any one of claims 1-4 in the manufacture of a medicament for the treatment of solid tumor cancer.

8. Use of a compound of any one of claims 1-4 in the manufacture of a medicament for the treatment of Downs syndrome or Alzheimer's disease.