Accordingly, there is a need for new therapies for treating insulin resistance, for example in type II diabetes patients.

Muscle wasting is a common complication of many prevalent diseases (e.g. cancer, heart failure, chronic obstructive lung disease, kidney failure, stroke) and a prominent feature of aging. Muscle loss causes weakness and limits mobility, thereby burdening both caregivers and the health care system. Severe loss of muscle mass results in death. Muscle wasting is an independent predictor of mortality in many conditions regardless of disease severity. In gastrointestinal cancers, at initial presentation, it is already present in 41% of patients, but often masked by obesity. This muscle wastage predicts not only death, but increased dose limiting toxicity to chemotherapy as well as earlier relapse [7]. High quality animal studies have demonstrated that treatment of muscle wasting in cancer cachexia prolongs survival independently of any effect on tumor burden [9]. Treatment of muscle atrophy may therefore not only improve quality of life, but also survival.

Despite the wide prevalence of muscle wasting and its important medical and social consequences, there are no approved therapies. Such a therapeutic would have a major impact on quality and span of life as well as reduce costs for assisted living and institutionalized care. There is therefore a need for an effective therapy for muscular atrophy.

SUMMARY

USPs are the largest subfamily of the deubiquitinating enzymes (DUBs) family with over 60 family members reported to date (Komander D. *et al*., *Nat. Rev. Mol.* (2009), 10, 550-563; Claque M. *et al*., *Physiol. Rev*. (2013), 93, 1289-1315).

Amongst all USPs, USP19 is an important member due to its implications in pathological conditions including but not restricted to muscle atrophy disorders, cancer, neurodegeneration and degenerative diseases as well as antiviral immune response. USP19 expresses as multiple isoforms varying in length from 71.09 kDa (isoform 2) to 156.03 kDa (isoform 5) with the canonical sequence (isoform 1) of 145.65 kDa in size (uniprot.org). The cellular localisation of USP19 may be cytosolic or bound to the endoplasmic reticulum (Lee J. *et al*., *J. Biol. Chem.* (2014), 289, 3510-3507; Lee J. *et al*., *Nat. Cell Biol.* (2016), 18, 765-776). Localised to the endoplasmic reticulum, USP19 is a key component of the endoplasmic reticulum-associated degradation (ERAD) pathway (Hassink B. *et al*., *EMBO J.* (2009), 10, 755-761; Lee J. *et al*., *J. Biol. Chem.* (2014), 289,

3510-3507; Lee J. *et al*., *Nat. Cell Biol.* (2016), 18, 765-776). In particular, USP19 is involved in the latter steps of the protein quality-control machinery rescuing ERAD substrates that have been retro-translocated to the cytosol. USP19 has also been demonstrated to regulate the stability of the E3 ligases MARCH6 and HRD1 (Nakamura N. *et al*., *Exp. Cell Res.* (2014), 328, 207-216; Harada K. *et al*., *Int. J. Mol. Sci.* (2016), 17, E1829). In addition, USP19 has recently been implicated in the stabilisation of multiple and potentially important protein substrates. For instance, USP19 interacts with SIAH proteins to rescue HIF1α from degradation under hypoxic conditions (Altun M. *et al*., *J. Biol. Chem*. (2012), 287, 1962-1969; Velasco K. *et al*., *Biochem. Biophys. Res. Commun*. (2013), 433, 390-395). USP19 also stabilises the KPC1 ubiquitin ligase which is involved in the regulation of the $p27^{Kip1}$ cyclin-dependent kinase inhibitor (Lu Y. *et al*., *Mol. Cell Biol*. (2009), 29, 547-558). Knock-out of USP19 by RNAi leads to $p27^{Kip1}$ accumulation and inhibition of cell proliferation (Lu L. *et al*., *PLoS ONE* (2011), 6,e15936). USP19 was also found to interact with the inhibitors of apoptosis (IAPs) including c-IAP1 and c-IAP2 (Mei Y. *et al*., *J. Biol. Chem*. (2011), 286, 35380-35387). Knockdown of USP19 decreases the total levels of these c-IAPs whilst overexpression increases the levels of both BIRC2/cIAP1 and BIRC3/cIAP2. Knockdown of USP19 also enhances TNFα-induced caspase activation and apoptosis in a BIRC2/c-IAP1 and BIRC3/c-IAP2 dependent manner. In addition to some direct involvement in regulating hypoxia response and ER stress, USP19 has also been implicated recently as a positive regulator of autophagy and negative regulator of type I interferon signalling (IFN, antiviral immune response) by deubiquitinating Beclin-1. USP19 was found to stabilise Beclin-1 at the post-translational level by removing the K11-linked ubiquitin chains of Beclin-1 at Lysine 437 (Jin S. *et al*., *EMBO J*. (2016), 35, 866-880). USP19 negatively regulates type I IFN signalling pathway, by blocking RIG-I-MAVS interaction in a Beclin-1 dependent manner. Depletion of either USP19 or Beclin-1 inhibits autophagic flux and promotes type I IFN signalling as well as cellular antiviral immunity (Jin S. *et al*., *EMBO J*. (2016), 35, 866-880; Cui J. *et al*., *Autophagy* (2016), 12, 1210-1211). Recent findings also indicate USP19 may negatively affect the cellular antiviral type I IFN signalling by regulating the TRAF3 substrate (Gu Z. *et al*., *Future Microbiol.* (2017), 12, 767-779) USP19 has also been recently implicated in the Wnt signalling pathway by stabilising the coreceptor LRP6 (Perrody E. *et al*., *eLife* (2016), 5, e19083) and in the DNA repair processes, most particularly chromosomal stability and integrity, by regulating the HDAC1 and HDAC2 proteins (Wu M. *et al*., *Oncotarget* (2017), 8, 2197-2208).

USP19 is also implicated in muscular atrophy, muscle-wasting syndromes and other skeletal muscle atrophy disorders (Wing S., *Int. J. Biochem. Cell Biol*. (2013), 45, 2130-2135; Wing S. *et al*., *Int. J. Biochem. Cell Biol*. (2016), 79, 426-468; Wiles B. *et al*., *Mol.*

Biol. Cell (2015), 26, 913-923; Combaret L. *et al.*, *Am. J. Physiol. Endocrinol. Metab.* (2005), 288, E693-700). This was supported for instance by studies which demonstrated that USP19-silencing induced the expression of myofibrillar proteins and promoted myogenesis (Sundaram P. *et al*., *Am. J. Physiol. Endocrinol. Metab*. (2009), 297, E1283-90; Ogawa M. *et al.*, *J. Biol. Chem*. (2011), 286, 41455-41465; Ogawa M. *et al*., *J. Endocrinol*. (2015), 225, 135-145).

In vivo studies have demonstrated that mice lacking the USP19 gene (USP19 KO mice) exhibited a decrease in fat mass when fed a high-fat diet (Coyne E, *et al*. *Diabetologia.* 2018 Nov 1. doi: 10.1007/s00125-018-4754-4., which is incorporated herein by reference). USP19 KO mice also exhibited greater glucose tolerance and higher insulin sensitivity when fed a high-fat diet.

These gene knock-out studies describe a connection between USP19 and obesity, as well as USP19 and insulin sensitivity. However, no *in vivo* studies have been described demonstrating that pharmacological inhibitors of USP19 are an effective approach to the treatment of obesity. Similarly, no *in vivo* studies have demonstrated that pharmacological inhibitors of USP19 can be effective in increasing insulin sensitivity.

Previous studies have demonstrated that mice lacking the USP19 gene (USP19 KO mice) were resistant to muscle wasting in response to both glucocorticoids, a common systemic cause of muscle atrophy, as well as in response to denervation, a model of disuse atrophy (Bedard N. *et al*., *FASEB J.* (2015), 29, 3889-3898, which is incorporated herein by reference).

These gene knock-out studies describe a connection between USP19 and muscular atrophy. However, no *in vivo* studies have been described demonstrating that pharmacological inhibitors of USP19 are an effective approach to the treatment of muscle-wasting conditions (e.g. cachexia and sarcopenia).

As set out in the accompanying Examples, it is demonstrated herein for the first time that pharmacological treatment with a USP19 inhibitor can induce therapeutic effects in a wild-type *in vivo* model. In particular, it is demonstrated for the first time that USP19 inhibitors reduce fat deposition in an *in vivo* model, indicating that USP19 inhibitors can be an effective treatment for obesity.

Similarly, it is demonstrated herein for the first time that USP19 inhibitors can reduce loss of muscle mass in an *in vivo* model of muscular atrophy.

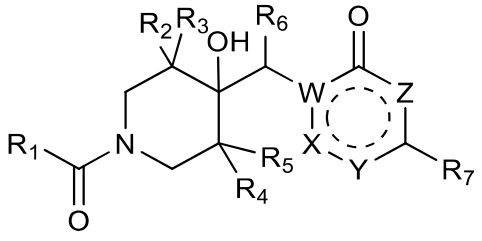
Similarly, it is demonstrated herein for the first time that USP19 inhibitors can treat the symptoms of insulin resistance, as indicated by an improved response to glucose.

WO2018/020242 provides for the first time a series of compounds which inhibit USP19, as determined by *in vitro* assay. The contents of WO2018/020242 are expressly incorporated herein by reference in its entirety, and particularly in relation to the compounds disclosed therein, their synthesis, methods of production and their *in vitro* inhibitory activity.

The Examples herein provide the first data demonstrating the efficacy of USP19 inhibitor compounds, for example those of WO2018/020242, in an *in vivo* model.

Thus, it is demonstrated in the accompanying Examples that the USP19 inhibitory compounds provided herein are capable of treating a number of disease conditions. Taken together, the *in vitro* and *in vivo* data demonstrate that compounds which potently inhibit USP19 activity can be effective therapeutic compounds.

In one aspect, the present disclosure provides use of a compound, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, in the manufacture of a medicament for the treatment of obesity, insulin resistance, or type II diabetes, wherein the compound is a compound according to formula (I):



(I)

wherein:

R_1 is an optionally substituted alkyl, alkenyl, alkynyl, ether, cycloalkyl, alkylcycloalkyl, heterocycloalkyl, alkylheterocycloalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl group;

R_2 is H or an optionally substituted alkyl group,

R_3 is H or an optionally substituted alkyl group,

R_4 is H or an optionally substituted alkyl group,

R_5 is H or an optionally substituted alkyl group,

R_2 and R_4 may be joined to one another to form an optionally substituted cycloalkyl or heterocycloalkyl that includes the carbon to which they are attached,

R_4 and R_5 may be joined to one another to form an optionally substituted cycloalkyl or heterocycloalkyl that includes the carbon to which they are attached;

R_6 is H or an optionally substituted alkyl group;

W is C or N;

X is N or CR_8, wherein R_8 is H or optionally substituted C1-C6 alkyl,

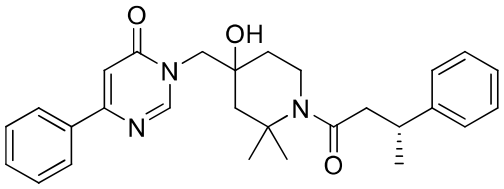
Y is N or CR_9

Z is CH, or NH,

wherein R_9 is H or optionally substituted alkyl, amido, amino, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, halo, carbonyl, ester, aminoalkyl, or cyano;

R_7 is hydrogen, halo, or an optionally substituted alkyl, alkenyl, alkynyl, amino, aryl, cycloalkyl, cycloalkenyl, alkoxy, aryloxy, heteroaryl or heterocycloalkyl group;

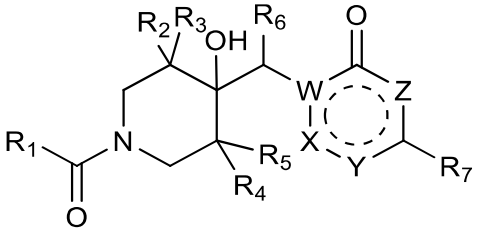
or the compound



or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof.

In another aspect, the present disclosure provides use of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined herein, in the manufacture of a medicament for the treatment of obesity, insulin resistance, or type II diabetes, optionally wherein the pharmaceutical composition further comprises a pharmaceutically acceptable diluent, excipient or carrier.

Accordingly, in a first example the disclosure provides a compound, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, for use in a method of therapy, wherein the compound is a compound according to formula (I):



(I)

wherein:

R_1 is an optionally substituted alkyl, alkenyl, alkynyl, ether, cycloalkyl, alkylcycloalkyl, heterocycloalkyl, alkylheterocycloalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl group;

R_2 is H or an optionally substituted alkyl group,

R_3 is H or an optionally substituted alkyl group,

R_4 is H or an optionally substituted alkyl group,

R_5 is H or an optionally substituted alkyl group,

R_2 and R_4 may be joined to one another to form an optionally substituted cycloalkyl or heterocycloalkyl that includes the carbon to which they are attached,

R_4 and R_5 may be joined to one another to form an optionally substituted cycloalkyl or heterocycloalkyl that includes the carbon to which they are attached;

R_6 is H or an optionally substituted alkyl group;

W is C or N;

X is N or CR_8, wherein R_8 is H or optionally substituted C1-C6 alkyl,

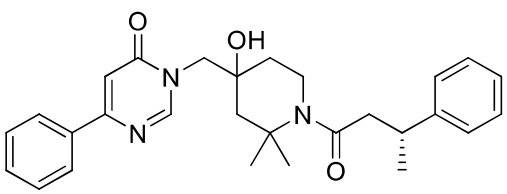
Y is N or CR_9

Z is CH, or NH,

wherein R_9 is H or optionally substituted alkyl, amido, amino, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, halo, carbonyl, ester, aminoalkyl, or cyano;

R_7 is hydrogen, halo, or an optionally substituted alkyl, alkenyl, alkynyl, amino, aryl, cycloalkyl, cycloalkenyl, alkoxy, aryloxy, heteroaryl or heterocycloalkyl group;

or the compound



or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof.

In a further example is provided a compound as defined in relation to the first example, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, for use in a method of treating obesity.

Also provided in accordance with the disclosure is a method of treating obesity comprising administering to a subject in need thereof an effective amount of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example, or an effective amount of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example.

In a further example of the disclosure is provided a compound as defined in relation to the first example of the disclosure, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, for use in a method of treating insulin resistance. In a further example of the disclosure is provided a compound as defined in relation to the first example of the disclosure, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, for use in a method of treating type II diabetes.

Also provided in accordance with the disclosure is a method of treating insulin resistance comprising administering to a subject in need thereof an effective amount of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure, or an effective amount of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure.

Also provided in accordance with the disclosure is a method of treating type II diabetes comprising administering to a subject in need thereof an effective amount of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure, or an effective amount of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure.

In a further example of the disclosure is provided a compound as defined in relation to the first example of the disclosure, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, for use in a method of treating muscular atrophy. In a further example the disclosure provides a compound as defined in relation to the first example, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, for use in a method of treating cachexia or sarcopenia.

Also provided in accordance with the disclosure is a method of treating muscular atrophy comprising administering to a subject in need thereof an effective amount of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure, or an effective amount of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure.

Also provided in accordance with the disclosure is a method of treating cachexia or sarcopenia comprising administering to a subject in need thereof an effective amount of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure, or an effective amount of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure.

It is further demonstrated herein that USP19 inhibitor compound as described in relation to the first example exhibit cell permeability and potent target engagement in cancer cell lines. The cell permeability and target engagement in cancer cells is comparable to that observed in muscle cells. As demonstrated herein, USP19 inhibitors exhibit potent *in vivo* therapeutic effects on muscle wasting. Thus, by extension, since similar target engagement is seen in cancer cells, it is expected that pharmacological USP19 inhibitors will be effective at exerting therapeutic effects in cancer, due to the association of USP19 and oncogenic processes described above.

Accordingly, in a further example of the disclosure is provided a compound as defined in relation to the first example of the disclosure, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, for use in a method of treating cancer.

Also provided in accordance with the disclosure is a method of treating cancer comprising administering to a subject in need thereof an effective amount of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure, or an effective amount of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in relation to the first example of the disclosure.

In preferred such examples the cancer to be treated in accordance with the disclosure is breast cancer or neuroblastoma.

The data presented herein is the first demonstration of the efficacy of USP19 inhibitors as effective therapeutic drugs. This efficacy is shown in a variety of pathological conditions. Accordingly, in a further example is provided a USP19 inhibitor for use in treating obesity. In a further example is provided a USP19 inhibitor for use in treating muscular atrophy. In a further example is provided a USP19 inhibitor for use in treating type II diabetes. In a further example is provided a USP19 inhibitor for use in treating cancer.

In a further example is provided a method of treating cancer, obesity, insulin resistance, type II diabetes and/or muscular atrophy comprising administering to a subject in need thereof an effective amount of a USP19 inhibitor.

Other preferred examples of the disclosure appear throughout the specification and in particular in the examples. Particularly preferred are those named compounds having greater activity as tested. Compounds having higher activity are more preferred over those having lower activity.

Each example or example as defined herein may be combined with any other example(s) or example(s) unless clearly indicated to the contrary. In particular any feature indicated as being preferred or advantageous may be combined with any other feature or features indicated as being preferred or advantageous.

FIGURES

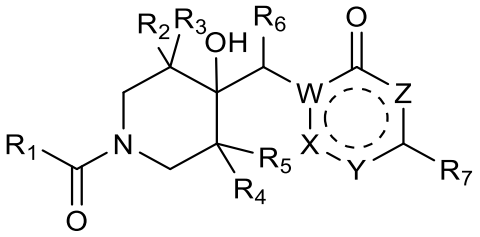
Figure 1: Effect of USP19 pharmacological inhibition on tibialis anterior mass. (A) Tibialis anterior mass (mg) from mice treated with vehicle or USP19 inhibitor compound ADC-141. Mass is given for the muscle from limb that had undergone sciatic nerve

denervation (DEN) and also from the innervated limb (INN). (B) Percentage loss of tibialis anterior muscle mass as a result of denervation in vehicle and USP19 inhibitor (ADC-141) treated mice. Percentage calculated as a proportion of the mass of the muscle from the innervated limb of the same mouse. (C) Loss of tibialis anterior muscle mass (in mg) as a result of denervation in vehicle treated and USP19 inhibitor (ADC-141) treated mice. P <0.025.

Figure 2: Effect of USP19 pharmacological inhibition on gastrocnemius muscle mass. (A) gastrocnemius muscle mass (mg) from mice treated with vehicle or USP19 inhibitor compound ADC-141. Mass is given for the muscle from limb that had undergone sciatic nerve denervation (DEN) and also from the innervated limb (INN). (B) Percentage loss of gastrocnemius muscle mass as a result of denervation in vehicle and USP19 inhibitor

CLAIMS:

1. Use of a compound, or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof, in the manufacture of a medicament for the treatment of obesity, insulin resistance, or type II diabetes, wherein the compound is a compound according to formula (I):



(I)

wherein:

R_1 is an optionally substituted alkyl, alkenyl, alkynyl, ether, cycloalkyl, alkylcycloalkyl, heterocycloalkyl, alkylheterocycloalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl group;

R_2 is H or an optionally substituted alkyl group,

R_3 is H or an optionally substituted alkyl group,

R_4 is H or an optionally substituted alkyl group,

R_5 is H or an optionally substituted alkyl group,

R_2 and R_4 may be joined to one another to form an optionally substituted cycloalkyl or heterocycloalkyl that includes the carbon to which they are attached,

R_4 and R_5 may be joined to one another to form an optionally substituted cycloalkyl or heterocycloalkyl that includes the carbon to which they are attached;

R_6 is H or an optionally substituted alkyl group;

W is C or N;

X is N or CR_8, wherein R_8 is H or optionally substituted C1-C6 alkyl,

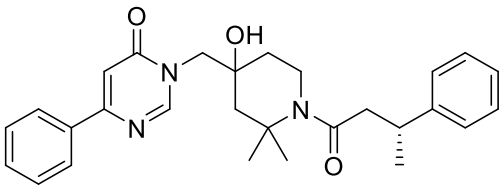
Y is N or CR_9

Z is CH, or NH,

wherein R_9 is H or optionally substituted alkyl, amido, amino, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, halo, carbonyl, ester, aminoalkyl, or cyano;

R_7 is hydrogen, halo, or an optionally substituted alkyl, alkenyl, alkynyl, amino, aryl, cycloalkyl, cycloalkenyl, alkoxy, aryloxy, heteroaryl or heterocycloalkyl group;

or the compound



or a pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof.

2. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to claim 1, wherein R_1 is optionally substituted C1-C6 alkyl, optionally substituted C4-C10 alkylcycloalkyl, optionally substituted C4-C5 heterocycloalkyl, optionally substituted C7-C10 arylalkyl, optionally substituted C3-C6 cycloalkyl, or optionally substituted C3-C6 heteroaryl,

wherein each optional substituent is independently selected from C1-C6 alkyl, C2-C6 alkenyl, hydroxymethyl, methoxymethyl, benzyloxy methyl, phenyl, C3-C6 cycloalkyl, CF_3, CHF_2, OH, or halo.

3. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to claim 1 or claim 2, wherein R_1 is optionally substituted C7-C10 cyclohexylalkane, optionally substituted C4-C6 cyclopropylalkane, optionally substituted C5-C6 cyclobutylalkane, optionally substituted C7-C10 alkylbenzene, optionally substituted 2,2 difluorobutane, or optionally substituted 3,3,3-trifluoropropane,

wherein each optional substituent is independently selected from C1-C6 alkyl, C2-C6 alkenyl, hydroxymethyl, hydroxyethyl, methoxymethyl, OH, or halo, optionally wherein R_1 is substituted and the substituent is C1-C6 alkyl, optionally methyl.

4. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any one of claims 1-3, wherein R_1 is methyl substituted cyclohexylethane or methyl substituted ethylbenzene, methyl substituted 2,2 difluorobutane, methyl substituted 3,3,3-trifluoropropane, C4-C5 heterocycloalkyl, or C4-C5 heterocycloalkyl substituted with phenyl

5. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to claim 4, wherein R_1 is phenyl-substituted pyrrolidine or phenyl-substituted piperidine.

6. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any of claims 1-5, wherein R_7 is optionally substituted C6-C10 aryl, C1-C12 heteroaryl, C1-C10 alkyl, C2-C10 alkenyl, C3-C10 cycloalkyl, amino, C1-C3 alkoxy, or halo,

wherein the optional substituent is selected from C1-C6 alkyl, hydroxysubstituted C1-C6 alkyl, C3-C6 cycloalkyl, C1-C6 heterocycloalkyl, C1-C6 alkoxy, halo-substituted C1-C6 alkoxy, amido, cyano or halo, optionally wherein R_7 is cyclopropyl, thiophene, or optionally substituted phenyl,

wherein the optional substituent is selected from C1-C6 alkyl, hydroxysubstituted C1-C6 alkyl, C1-C6 alkylamine, and halo, optionally wherein R_7 is phenyl or fluoro-substituted phenyl.

7. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any of claims 1-6, wherein R_2, R_3, R_4, R_5 are independently selected from H and C1-C6 alkyl, optionally wherein R_2 and R_3 are H, and R_4 and R_5 are methyl.

8. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any of claims 1-7 wherein R_4 and R_5 are joined to one another to form an optionally substituted C3-C6 cycloalkyl or C3-C6 heterocycloalkyl that includes the carbon to which they are attached and R_2 and R_3 are independently selected from H and C1-C6 alkyl, optionally wherein R_2 and R_3 are H and R_4 and R_5 are joined to one another to form a C3-C6 cycloalkyl that includes the carbon to which they are attached.

9. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to claim 8, wherein R_4 and R_5 are joined to one another to form a C4 or C5 cycloalkyl that includes the carbon to which they are attached.

10. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any one of claims 1-9 wherein R_6 is H or C1-C6 alkyl.

11. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any of claims 1-6, wherein R_2 and R_4 are joined to one another to form a C5 cycloalkyl that includes the carbons to which they are attached, and wherein R_3, R_5 and R_6 are independently H or C1-C6 alkyl.

12. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any of claims 1-11, wherein W is N and X is CR_8, wherein R_8 is H or methyl.

13. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any of claims 1-12, wherein Y is N or CR_9, wherein R_9 is H, C1-C6 alkyl, NR'R'', C(O)NR'R'', cyano, carboxyl, halo, C1-C6 alkylamine, C3-C6 alkylester, optionally substituted C6-C10 aryl or optionally substituted C2-C6 heteroaryl, wherein the one or more heteroatoms are selected from N and O, and the one or more optional substituents of the aryl or heteroaryl are selected from C1-C6 alkyl, C1-C6 alkylamine, amido, and cyano,

wherein R' and R'' are independently selected from H, C1-C6 alkyl optionally substituted with OH, C3-C7 cycloalkyl, C1-C7 heterocycloalkyl, C4-C7 alkylcycloalkyl, C3-C7 alkylheterocycloalkyl, benzyl, phenyl, and methoxy, or wherein R' and R'' are joined to one another to form a C2-C7 heterocycle that includes the N to which they are attached, wherein the heterocycle is optionally hydroxyl-substituted, oxo-substituted, methyl-substituted, CH2OH-substituted, or acetyl-substituted.

14. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any of claims 1-13, wherein Y is N or CR_9, wherein R_9 is selected from: phenyl optionally substituted with amido, cyano or methyl amine; pyridine; oxazole; pyrazole; carboxyl; C(O)NR'R''; or NR'R'';

wherein R' and R'' are independently selected from H, C1-C6 alkyl, C3-C7 cycloalkyl, C3-C7 heterocycloalkyl wherein the heteroatom is N or O, or wherein R' and R'' are joined to one another to form a C2-C7 heterocycloalkyl that includes the N to which they are attached, wherein the heterocycloalkyl is optionally hydroxyl-substituted, oxo-substituted, methyl-substituted, CH2OH-substituted, or acetyl-substituted.

15. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to claim 1, wherein

R_1 is selected from optionally substituted ethylcyclohexane, optionally substituted ethylbenzene, optionally substituted 2,2 difluorobutane, and optionally substituted 3,3,3-trifluoropropane, wherein the optional substituent is one or more of methyl, ethyl, propyl, propenyl, hydroxymethyl and methoxymethyl, or wherein R_1 is phenyl-substituted pyrrolidine;

R_2 and R_3 are independently selected from H, methyl,

R_4 and R_5 are independently selected from H, methyl, or are joined to one another to form a C3-C6 cycloalkyl or heterocycloalkyl that includes the carbon to which they are attached, optionally a C4 or C5 cycloalkyl that includes the carbon to which they are attached

R_6 is H or methyl,

R_7 is selected from optionally substituted phenyl, indazole, thiophene, or pyrazole, wherein the optional substituent is selected from C1-C6 alkyl, hydroxysubstituted C1-C6 alkyl, C3-C6 cycloalkyl, C1-C6 heterocycloalkyl, C1-C6 alkoxy, halo-substituted C1-C6 alkoxy, C1-C6 alkylamine, amido, cyano or halo,

W is N or C

X is CH or N

Z is C or NH

Y is N or CR_9, wherein R_9 is selected from: phenyl optionally substituted with amido, cyano or methyl amine; pyridine; oxazole; pyrazole; C(O)NR'R''; or NR'R'';

wherein R' and R'' are independently selected from H, C1-C6 alkyl, C3-C7 cycloalkyl, C3-C7 heterocycloalkyl wherein the heteroatom is N or O, or wherein R' and R'' are joined to one another to form a C2-C7 heterocycloalkyl that includes the N to which they are attached, wherein the heterocycloalkyl is optionally hydroxyl-substituted, oxo-substituted, methyl-substituted, hydroxymethyl-substituted, or acetyl-substituted.

16. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any one of claims 13-15, wherein Y is CR_9, wherein R_9 is C(O)NR'R'' and wherein R' and R'' are joined to one another to form an optionally substituted pyrrolidine, piperidine, piperazine or morpholine that includes the N to which they are attached, wherein the piperidine, pyrrolidine, piperazine or morpholine is optionally hydroxyl-substituted, oxo-substituted, methyl-substituted, hydroxymethyl-substituted, or acetyl-substituted, optionally wherein Y is CR_9, wherein R_9 is C(O)NR'R'' and wherein R' and R'' are joined to one another to form a piperazinyl ring.

17. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any one of claims 1-15 wherein W is N and Y is N, such that the ring comprising W, X, Y, Z is a substituted pyrimidinone ring.

18. The use of a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative according to any one of claims 1-17 wherein when the compound is chiral at the hydroxyl position of formula (I), the compound is the *S* enantiomer.

19. The use of a compound, or pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative thereof according to claim 1, wherein the compound is:

(*R*)-5-Bromo-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenylpyridin-2(1*H*)-one;

6-(2-Fluorophenyl)-3-((4-hydroxy-1-(3-phenylpropanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

3-((1-(3-Cyclobutylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

3-((1-(3-Cyclopentylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-6-(2-Fluorophenyl)-3-((4-hydroxy-1-(2-methyl-3-phenylpropanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*)-*N*-(3-(1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridin-3-yl)phenyl)acetamide;

(*R*)-3-(1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)6-oxo-4-phenyl-1,6-dihydropyridin-3-yl)benzamide;

(*R*)-5-(Furan-2-yl)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenylpyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-(1-methyl-1*H*-pyrazol-5-yl)-4-phenylpyridin-2(1*H*)-one;

(*R*)-4-Chloro-1-((4-hydroxy-1(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-phenylpyridin-2(1*H*)-one;

(*R*)-4-(Dimethylamino)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-phenylpyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-phenyl-4-(prop-1-en-2-yl)pyridine-2(1*H*)-one;

(*R*)-Ethyl 1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylate;

(*R,S*)-4-(2-Fluorophenyl)-1-((4-hydroxy-1-(2-methyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

(*R*,*S*)-1-((1-(3-Cyclobutyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-4-phenyl-5-(piperidine-1-carbonyl)pyridin-2(1*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(1-methyl-1*H*-indazol-7-yl)pyrimidin-4(3*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(2-methoxyphenyl)pyrimidin-4(3*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-2-methyl-6-phenylpyrimidin-4(3*H*)-one;

(*R*)-2-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5,6-diphenylpyridazin-3(2*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(naphthalen-1-yl)pyrimidin-4(3*H*)-one;

(*R*)-6-(3-(1,3-Dioxolan-2-yl)phenyl)-3-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(thiophen-3-yl)pyrimidin-4(3*H*)-one;

4-(2-Fluorophenyl)-1-((4-hydroxy-1-(1-methylcyclopentane-1-carbonyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

3-((1-(1-Ethylcyclohexane-1-carbonyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

3-((1-(2-(Cyclohexylmethyl)-3-methylbutanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*)-6-(Furan-2-yl)-3-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenylpyridin-2(1*H*)-one;

(*R*)-6-(Cyclohex-1-en-1-yl)-3-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(prop-1-en-2-yl)pyrimidin-4(3*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(2-(trifluoromethoxy)phenyl)pyrimidin-4(3*H*)-one;

3-(((1*R*,5*S*)-3-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-8-hydroxy-3-azabicyclo[3.2.1]octan-8-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*)-6-(2-Fluorophenyl)-3-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*)-5-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-2-phenylpyrimidin-4(3*H*)-one;

3-((4-Hydroxy-1-(3-phenylpropanoyl)piperidin-4-yl)methyl)-2-methyl-6-phenylpyrimidin-4(3*H*)-one;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(isobutylamino)pyrimidin-4(3*H*)-one;

(*R*)-1-((1-(3-Cyclohexyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-4-phenyl-5-(piperidine-1-carbonyl)pyridin-2(1*H*)-one;

(*R*)-2-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-phenylpyridazin-3(2*H*)-one;

(*R*)-4-(2-Cyanophenyl)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

(*R*)-3-((1-(3-Cyclohexyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

3-((1-(2-(Cyclohexylmethyl)butanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

rac-6-(2-Fluorophenyl)-3-((4-hydroxy-1-(*cis*-2-phenylcyclopropanecarbonyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

6-(2-Fluorophenyl)-3-((4-hydroxy-1-(1-methylcyclohexanecarbonyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

3-((*S*)-1-(1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)propyl)-6-phenylpyrimidin-4(3*H*)-one;

3-((*R*)-1-(1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)propyl)-6-phenylpyrimidin-4(3*H*)-one;

(*R*,*S*)-3-((1-(3-Cyclohexyl-2-hydroxypropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carbaldehyde;

(*R*)-5-((Dimethylamino)methyl)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenylpyridin-2(1*H*)-one;

3-((*R*)-1-(4-Hydroxy-1-((*R*)-3-phenylbutanoyl)piperidin-4-yl)ethyl)-6-phenylpyrimidin-4(3*H*)-one;

3-((*S*)-1-(4-Hydroxy-1-((*R*)-3-phenylbutanoyl)piperidin-4-yl)ethyl)-6-phenylpyrimidin-4(3*H*)-one;

(*R*)-6-(2-Fluorophenyl)-3-((4-hydroxy-1-(4,4,4-trifluoro-3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-3-((1-(3-Cyclohexyl-2-fluoropropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

3-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*R*)-6-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-9-hydroxy-6-azaspiro[3.5]nonan-9-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

3-(((*S*)-6-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-9-hydroxy-6-azaspiro[3.5]nonan-9-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*)-5-(3-(Aminomethyl)phenyl)-1-((1-(3-cyclohexyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-4-(2-fluorophenyl)pyridin-2(1*H*)-one;

3-(((*S*)-4-Hydroxy-3,3-dimethyl-1-((*R*)-3-phenylbutanoyl)piperidin-4-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*R*)-4-Hydroxy-3,3-dimethyl-1-((*R*)-3-phenylbutanoyl)piperidin-4-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

(*R*)-6-(4-Fluorophenoxy)-3-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-(2-oxopyrrolidin-1-yl)-4-phenylpyridin-2(1*H*)-one;

6-(2-Fluorophenyl)-3-((4-hydroxy-1-(1-methyl-4-methylenecyclohexanecarbonyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-3-((1-(3-Cyclobutyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R,S*)-3-((1-(3-Cycloheptyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

3-((1-(3-Cyclobutyl-2,2-dimethylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

6-(2-Fluorophenyl)-3-(((1*R*,5*S*)-8-hydroxy-3-((*R*)-3-phenylbutanoyl)-3-azabicyclo[3.2.1]octan-8-yl)methyl)pyrimidin-4(3*H*)-one;

3-(((*R*)-4-Hydroxy-2,2-dimethyl-1-((*R*)-3-phenylbutanoyl)piperidin-4-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*S*)-4-Hydroxy-2,2-dimethyl-1-((*R*)-3-phenylbutanoyl)piperidin-4-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-(4-hydroxypiperidine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenyl-5-(pyrrolidine-1-carbonyl)pyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenyl-5-(1,4-dioxa-8-azaspiro[4.5]decane-8-carbonyl)pyridin-2(1*H*)-one;

(*R*)-*N*-Cyclohexyl-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

6-(2-Fluorophenyl)-3-((4-hydroxy-3,3-dimethyl-1-(*cis*-2-phenylcyclopropane-1-carbonyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-3-((1-(3-Cyclohexyl-1H-pyrazole-4-carbonyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-6-(2-Fluorophenyl)-3-((4-hydroxy-3,3-dimethyl-1-(3-phenylpropanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-6-(2-Fluorophenyl)-3-((4-hydroxy-1-(1-isobutyl cyclopropane-1-carbonyl)-3,3-dimethylpiperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R,S*)-6-(2-Fluorophenyl)-3-((4-hydroxy-3,3-dimethyl-1-(3-methyl-3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*S*)-1-((1-(4,4-Difluoro-3-phenylbutanoyl)-4-hydroxypiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((4-Hydroxy-1-(1-(thiophen-2-yl)cyclopropane-1-carbonyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-3-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-(2-(hydroxymethyl)phenyl)pyrimidin-4(3*H*)-one;

(*R*)-*N*,*N*-Diethyl-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

3-((1-(3-Cyclohexylbutanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

(*R*,*S*)-3-((1-(3-Cyclohexylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-1-((1-(3-Cyclobutylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*,*S*)-1-((1-(2-Ethylhexanoyl)-4-hydroxypiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R,S*)-6-(2-Fluorophenyl)-3-((4-hydroxy-3,3-dimethyl-1-(1-methylcyclohexane-1-carbonyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

6-(2-Fluorophenyl)-3-((1-(3-(4-fluorophenyl)propanoyl)-4-hydroxypiperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

(*R*,*S*)-3-((1-(3-Cyclopropylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

1-((1-(2,2-Dimethylbutanoyl)-4-hydroxypiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-*N*-(2-(1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-1,6-dihydropyrimidin-4-yl)phenyl)acetamide;

(*R*)-5-(4-(Aminomethyl)phenyl)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenylpyridin-2(1*H*)-one;

(*R*)-1-((1-(3-Cyclohexyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenyl-5-(piperidine-1-carbonyl)pyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-isopropyl-4-(2-methoxyphenyl)-*N*-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

(*R*)-4-(2-Fluorophenyl)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

(*R*)-1'-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4'-phenyl-[2,3'-bipyridin]-6'(1'*H*)-one;

1-((1-(3-Cyclohexylpropanoyl)-4-hydroxypiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-*tert*-Butyl 4-(1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carbonyl)piperazine-1-carboxylate;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-(*p*-tolyl)-1,6-dihydropyridine-3-carboxamide;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-methoxy-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4,5-diphenylpyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenyl-[3,3'-bipyridin]-6(1*H*)-one;

(*R*)-5-(3-(Aminomethyl)phenyl)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenylpyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-(*m*-tolyl)-1,6-dihydropyridine-3-carboxamide;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-4-phenyl-5-(pyrimidin-5-yl)pyridin-2(1*H*)-one;

(*R*)-*N*-(Cyclopropylmethyl)-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-*N*-Benzyl-1-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-2-(1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridin-3-yl)benzonitrile;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-methyl-6-oxo-*N*,4-diphenyl-1,6-dihydropyridine-3-carboxamide;

3-(1-(1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxypiperidin-4-yl)ethyl)-6-phenylpyrimidin-4(3*H*)-one;

(R)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-(1-methyl-1H-pyrazol-4-yl)-4-phenylpyridin-2(1H)-one;

(*R*)-3-((1-(2-(Cyclohexylmethyl)pent-4-enoyl)-4-hydroxypiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-methyl-4-phenylpyridin-2(1*H*)-one;

(*R*)-6-(1,5-Dimethyl-1*H*-pyrazol-4-yl)-3-((4-hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

3-(((1*R*,5*S*)-3-(3-Cyclohexylpropanoyl)-8-hydroxy-3-azabicyclo[3.2.1]octan-8-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carbonitrile;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-*N*-(2-hydroxyethyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((4-Hydroxy-1-((*R*)-3-phenylbutanoyl)piperidin-4-yl)methyl)-5-((*S*)-2-methylpyrrolidine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-1-(3-phenylbutanoyl)piperidin-4-yl)methyl)-5-(4-(hydroxymethyl)piperidine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

3-((1-(2-(Cyclohexylmethyl)butanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

3-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-phenyl-5-(pyrrolidine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

3-((1-(2-(Cyclohexyloxy)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

1-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-((1-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((1-((*R*)-3-Cyclopropyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-[4,5'-bipyrimidin]-6(1*H*)-one;

3-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(1-methyl-1*H*-pyrazol-5-yl)pyrimidin-4(3*H*)-one;

3-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(1*H*-pyrazol-4-yl)pyrimidin-4(3*H*)-one;

3-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(1*H*-pyrazol-5-yl)pyrimidin-4(3*H*)-one;

3-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)pyrimidin-4(3*H*)-one;

3-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(thiophen-3-yl)pyrimidin-4(3*H*)-one;

1-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-(oxazol-2-yl)-4-phenylpyridin-2(1*H*)-one;

3-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-(hydroxymethyl)phenyl)pyrimidin-4(3*H*)-one;

3-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(3-(hydroxymethyl)phenyl)pyrimidin-4(3*H*)-one;

3-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(4-(hydroxymethyl)phenyl)pyrimidin-4(3*H*)-one;

6-(4-(Aminomethyl)phenyl)-3-((1-((*R*)-3-cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

6-(2-(Aminomethyl)phenyl)-3-((1-((*R*)-3-cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

6-(2-Fluorophenyl)-3-((4-hydroxy-3,3-dimethyl-1-(2,4,4-trimethylpentanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

6-(2-Fluorophenyl)-3-((4-hydroxy-3,3-dimethyl-1-(4,4,4-trifluoro-2-methylbutanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

4-Chloro-1-((7-((*R*)-3-cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(dimethylamino)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-((1-((*S*)-3-(Benzyloxy)-2-(cyclohexylmethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-isobutyryl-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-((*R*)-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-((*R*)-3-Cyclopropyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

6-(2-Fluorophenyl)-3-((4-hydroxy-3,3-dimethyl-1-(2-methyl-3-(1*H*-pyrazol-1-yl)propanoyl)piperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

1-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-(hydroxymethyl)phenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*S*)-3-Cyclohexyl-2-(hydroxymethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*S*)-3-Cyclohexyl-2-(hydroxymethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1’-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4'-(2-fluorophenyl)-[2,3'-bipyridin]-6'(1'*H*)-one;

1-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-(thiophen-3-yl)-1,6-dihydropyridine-3-carboxamide;

1-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(3-(hydroxymethyl)phenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-((7-(3-Cyclohexyl-2-hydroxypropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(2-methyl-3-(piperidin-1-yl)propanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

6-(3-(Aminomethyl)phenyl)-3-((1-((*R*)-3-cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)pyrimidin-4(3*H*)-one;

1-(((*S*)-1-((*S*)-3-Cyclohexyl-2-(methoxymethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

4-(2-(Aminomethyl)phenyl)-1-((7-((*R*)-3-cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(4-(hydroxymethyl)phenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(2-methyl-3-morpholinopropanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*S*)-2-(Cyclohexylmethyl)-4-hydroxybutanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*S*)-2-(Cyclohexylmethyl)-4-hydroxybutanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*S*)-3-Cyclobutyl-2-(hydroxymethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*S*)-3-Cyclobutyl-2-(hydroxymethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

5-(4-Acetylpiperazine-1-carbonyl)-1-((1-((*R*)-3-cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-phenylpyridin-2(1*H*)-one;

1-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-(4-methylpiperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-((10-Hydroxy-7-(4,4,4-trifluoro-3-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(4,4,4-trifluorobutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(3-(tetrahydrofuran-3-yl)propanoyl)-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-((1*R*,2*S*)-2-phenylcyclopropane-1-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(Cyclopropanecarbonyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(1-methylcyclohexane-1-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(3-Fluorocyclopentane-1-carbonyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(1-(2,2-Difluoroethyl)cyclopropane-1-carbonyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(Bicyclo[2.2.1]heptane-1-carbonyl)-10-hydroxy-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-((*S*)-4,4-Difluoro-3-phenylbutanoyl)-10-hydroxy-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-((*R*)-4,4-Difluoro-3-phenylbutanoyl)-10-hydroxy-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(3-Ethoxypropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-((*S*)-3-phenylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(3-(4-Fluorophenyl)propanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-((*R*)-3-phenylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(1-methylcyclopentane-1-carbonyl)-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(1*H*-pyrazole-3-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(1*H*-indazole-3-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(3-Cyclohexyl-1*H*-pyrazole-4-carbonyl)-10-hydroxy-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(1*H*-indole-3-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(Bicyclo[1.1.1]pentane-1-carbonyl)-10-hydroxy-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(5-phenyloxazole-4-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(5-Cyclopropyloxazole-4-carbonyl)-10-hydroxy-7-azaspiro [4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(2-(Cyclohexyloxy)acetyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(spiro[2.2]pentane-1-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(3-(trifluoromethyl)cyclopentane-1-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(2,4-Dimethylpentanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(1-Benzyl-1*H*-pyrrole-2-carbonyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(2-(Cyclohexyloxy)propanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

3-((1-((*S*)-3-Cyclobutyl-2-(hydroxymethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-(2-fluorophenyl)pyrimidin-4(3*H*)-one;

1-((7-(2-Cyclobutoxyacetyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(3,3-Difluorocyclopentane-1-carbonyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(2-hydroxy-3-phenylpropanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-4-Hydroxy-3,3-dimethyl-1-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)piperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

(*S*)-1-((4-Hydroxy-3,3-dimethyl-1-(4,4,4-trifluoro-2-(2,2,2-trifluoroethyl)butanoyl)piperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-((*S*)-2-(hydroxymethyl)piperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-((*R*)-3-methylpiperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*S*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

(*S*)-1-((10-Hydroxy-7-(4,4,4-trifluoro-2-(2,2,2-trifluoroethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*S*)-1-((10-Hydroxy-7-(4,4,4-trifluoro-2-(2,2,2-trifluoroethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-cyclopropyl-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-cyclopropyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

4-(2-Fluorophenyl)-1-(((*S*)-10-hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

4-(2-Fluorophenyl)-1-(((*S*)-10-hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-(4-hydroxypiperidine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-((10-Hydroxy-7-(3-(trifluoromethyl)cyclobutane-1-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-((2-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-5-hydroxy-9-oxa-2-azaspiro[5.5]undecan-5-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-1-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-((2-((*R)*-3-Cyclohexyl-2-methylpropanoyl)-5-hydroxy-2-azaspiro[5.5]undecan-5-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((2-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-5-hydroxy-2-azaspiro[5.5]undecan-5-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-5-(4-methylpiperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-((1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylic acid;

1-((7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-methoxy-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-((7-(4,4-Difluoro-2-methylbutanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((7-(4,4-Difluoro-2,2-dimethylbutanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(4-(trifluoromethyl)thiazole-2-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-((10-Hydroxy-7-(2-(trifluoromethyl)thiazole-4-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-10-Hydroxy-7-((*S*)-4,4,4-trifluoro-2-(hydroxymethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*S*)-10-Hydroxy-7-((*S*)-4,4,4-trifluoro-2-(hydroxymethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*S*)-10-Hydroxy-7-((*S*)-4,4,4-trifluoro-2-(hydroxymethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*S*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*S*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(4-methylpiperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

Ethyl 1-(((*S*)-7-((*R*)-3-cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylate;

1-(((*S*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylic acid;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*-isopropyl-*N*-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-phenyl-5-(pyrrolidine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-1-((*S*)-3-Cyclohexyl-2-(methoxymethyl)propanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-4-Hydroxy-3,3-dimethyl-1-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)piperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

(*R*)-1-((4-Hydroxy-3,3-dimethyl-1-(4,4,4-trifluoro-2-(2,2,2-trifluoroethyl)butanoyl)piperidin-4-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-((*S*)-2-(hydroxymethyl)piperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-((*R*)-3-methylpiperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

(*R*)-1-((10-Hydroxy-7-(4,4,4-trifluoro-2-(2,2,2-trifluoroethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

(*R*)-1-((10-Hydroxy-7-(4,4,4-trifluoro-2-(2,2,2-trifluoroethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-cyclopropyl-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-cyclopropyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

4-(2-Fluorophenyl)-1-(((*R*)-10-hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

4-(2-Fluorophenyl)-1-(((*R*)-10-hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-1-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-5-(4-hydroxypiperidine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-7-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-4-cyclopropyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-1-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-*N*,*N*-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-1-((*R*)-3-Cyclobutyl-2-methylpropanoyl)-4-hydroxy-3,3-dimethylpiperidin-4-yl)methyl)-4-(2-fluorophenyl)-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-5-(4-methylpiperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-10-Hydroxy-7-((*S*)-4,4,4-trifluoro-2-(hydroxymethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-*N*,*N*-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxamide;

1-(((*R*)-10-Hydroxy-7-((*S*)-4,4,4-trifluoro-2-(hydroxymethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-10-Hydroxy-7-((*S*)-4,4,4-trifluoro-2-(hydroxymethyl)butanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-4-phenyl-5-(piperazine-1-carbonyl)pyridin-2(1*H*)-one;

1-(((*R*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(morpholine-4-carbonyl)-4-phenylpyridin-2(1*H*)-one;

1-(((*R*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-5-(4-methylpiperazine-1-carbonyl)-4-phenylpyridin-2(1*H*)-one;

Ethyl 1-(((*R*)-7-((*R*)-3-cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylate;

1-(((*R*)-7-((*R*)-3-Cyclohexyl-2-methylpropanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylic acid;

3-((10-Hydroxy-7-((3*R*,4*R*)-3-phenylpiperidine-4-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*S*)-10-Hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

6-(2-Fluorophenyl)-3-(((*S*)-10-hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)pyrimidin-4(3*H*)-one;

6-(3-Fluorophenyl)-3-(((*S*)-10-hydroxy-7-((*R*)-4,4,4-trifluoro-2-methylbutanoyl)-7-azaspiro[4.5]decan-10-yl)methyl)pyrimidin-4(3*H*)-one;

3-(((*S*)-7-((*R*)-4,4-Difluoro-2-methylpentanoyl)-10-hydroxy-7-azaspiro[4.5]decan-10-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*S*)-10-Hydroxy-7-((3*S*,4*R*)-4-phenylpyrrolidine-3-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*S*)-10-Hydroxy-7-((3*R*,4*S*)-4-phenylpyrrolidine-3-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*S*)-10-Hydroxy-7-((2*R*,3*R*)-2-phenylpyrrolidine-3-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one;

3-(((*S*)-10-Hydroxy-7-((2*S*,3*S*)-2-phenylpyrrolidine-3-carbonyl)-7-azaspiro[4.5]decan-10-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one.

20. Use of a pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, tautomer, stereoisomer or *N*-oxide derivative as defined in any one of claims 1-19, in the manufacture of a medicament for the treatment of obesity, insulin resistance, or type II diabetes, optionally wherein the pharmaceutical composition further comprises a pharmaceutically acceptable diluent, excipient or carrier.