GPR119 RECEPTOR AGONISTS IN METHODS OF INCREASING BONE MASS AND OF TREATING OSTEOPOROSIS AND OTHER CONDITIONS CHARACTERIZED BY LOW BONE MASS, AND COMBINATION THERAPY RELATING THERETO

FIELD OF THE INVENTION

The present invention relates to the use of GPR119 receptor agonists for treating or preventing a condition characterized by low bone mass, such as osteoporosis, and for increasing bone mass in an individual. The present invention further relates to the use of a GPR119 receptor agonist in combination with a dipeptidyl peptidase IV (DPP-IV) inhibitor for treating or preventing a condition characterized by low bone mass, such as osteoporosis, and for increasing bone mass in an individual. A GPR119 receptor agonist and the combination of a GPR119 receptor agonist and a DPP-IV inhibitor promote bone formation in an individual.

BACKGROUND OF THE INVENTION

The following discussion is intended to facilitate the understanding of the invention, but is not intended nor admitted to be prior art to the invention.

A. Osteoporosis

Osteoporosis is a disabling disease characterized by the loss of bone mass and microarchitectural deterioration of skeletal structure leading to compromised bone strength, which predisposes a patient to increased risk of fragility fractures. Osteoporosis affects more than 75 million people in Europe, Japan and the United States, and causes more than 2.3 million fractures in Europe and the United States alone. In the United States, osteoporosis affects at least 25% of all post-menopausal white women, and the proportion rises to 70% in women older than 80 years. One in three women older than 50 years will have an osteoporotic fracture that causes a considerable social and financial burden on society. The disease is not limited to women; older men also can be affected. By 2050, the worldwide incidence of hip fracture in men is projected to increase by 310% and 240% in women. The combined lifetime risk for hip, forearm, and vertebral fractures presenting clinically is around 40%, equivalent to the risk for cardiovascular disease. Osteoporotic fractures therefore cause substantial mortaility, morbidity, and economic cost. With an ageing population, the number of osteoporotic fractures and their costs will at least double in the next 50 years unless effective preventive strategies are developed. (See, e.g., Atik et al., Clin Orthop Relat Res (2006) 443:19-24; Raisz, J Clin Invest (2005) 115:3318-3325; and World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis.)

B. Glucose-dependent Insulinotropic Polypeptide (GIP)

Glucose-dependent insulinotropic polypeptide (GIP, also known as gastric inhibitory polypeptide) is a peptide incretin hormone of 42 amino acids that is released from duodenal endocrine

K cells after meal ingestion. The amount of GIP released is largely dependent on the amount of glucose consumed. GIP has been shown to stimulate glucose-dependent insulin secretion in pancreatic beta cells. GIP mediates its actions through a specific G protein-coupled receptor, namely GIPR.

As GIP contains an alanine at position 2, it is an excellent substrate for dipeptidyl peptidase-4 (DPP-IV), an enzyme regulating the degradation of GIP. Full-length GIP(1-42) is rapidly converted to bioinactive GIP(3-42) within minutes of secretion from the gut K cell. Inhibition of DPP-IV has been shown to augment GIP bioactivity. (See, *e.g.*, Drucker, Cell Metab (2006) 3:153-165; McIntosh et al., Regul Pept (2005) 128:159-165; Deacon, Regul Pept (2005) 128:117-124; and Ahren et al., Endocrinology (2005) 146:2055-2059.). Analysis of full length bioactive GIP, for example in blood, can be carried out using N-terminal-specific assays (see, e.g., Deacon et al, J Clin Endocrinol Metab (2000) 85:3575-3581).

Recently, GIP has been shown to promote bone formation. GIP has been shown to activate osteoblastic receptors, resulting in increases in collagen type I synthesis and alkaline phosphatase activity, both associated with bone formation. GIP has been shown to inhibit osteoclast activity and differentiation *in vitro*. GIP administration has been shown to prevent the bone loss due to ovariectomy. GIP receptor (GIPR) knockout mice evidence a decreased bone size, lower bone mass, altered bone microarchitecture and biochemical properties, and altered parameters for bone turnover, especially in bone formation. (See, e.g., Zhong et al, Am J Physiol Endocrinol Metab (2007) 292:E543-E548; Bollag et al., Endocrinology (2000) 141:1228-1235; Bollag et al., Mol Cell Endocrinol (2001) 177:35-41; Xie et al., Bone (2005) 37:759-769; and Tsukiyama et al., Mol Endocrinol (2006) 20:1644-1651.)

The usefulness of GIP for maintaining or increasing bone density or formation has been acknowledged by the United State Trademark and Patent Office by issuance of United States Patent No. 6,410,508 for the treatment of reduced bone mineralization by administration of GIP peptide. However, current GIP peptide agonists suffer from a lack of oral bioavailability, negatively impacting patient compliance. An attractive alternative approach is to develop an orally active composition for increasing an endogenous level of GIP activity.

C. GPR119

GPR119 is a G protein-coupled receptor (GPR119; *e.g.*, human GPR119, GenBank® Accession No. AAP72125 and alleles thereof; *e.g.*, mouse GPR119, GenBank® Accession No. AY288423 and alleles thereof). GPR119 activation as by an agonist leads to elevation of the level of intracellular cAMP, consistent with GPR119 being coupled to Gs. In the patent literature, GPR119 has been referred to as RUP3 (*e.g.*, International Application No. PCT/US99/23687); GPR119 has also been referred to as Glucose-Dependent Insulinotropic Receptor (GDIR).

D. Dipeptidyl Peptidase IV (DPP-IV)

Dipeptidyl peptidase IV (DPP-IV, EC 3.4.14.5) exhibits catalytic activity against a broad range of peptide substrates that includes peptide hormones, neuropeptides, and chemokines. The incretins glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), which stimulate glucose-dependent insulin secretion and otherwise promote blood glucose homeostasis, are rapidly cleaved by DPP-IV at the position 2 alanine leading to inactivation of their biological activity. Both pharmacological and genetic attenuation of DPP-IV activity are associated with enhanced incretin action *in vivo*. A second-generation DPP-IV inhibitor, LAF237 (vildagliptin) (Ahren et al., J Clin Endocrinol Metab (2004) 89:2078-2084; and Villhauer et al., J Med Chem (2003) 46:2774-2789; the disclosure of each of which is herein incorporated by reference in its entirety), is currently in phase 3 clinical trials for Type 2 diabetes and additional DPP-IV inhibitors are in clinical development, including MK-0431 (sitagliptin), BMS-477118 (saxagliptin), PSN-9301, T-6666, PHX-1149 and SYR-322 (alogliptin). Sitagliptin (Januvia™; sitagliptin phosphate) has recently been approved by the U.S. Food and Drug Administration for use to improve blood sugar levels in patients with Type 2 diabetes.

Because the incretin hormones are not the only substrates for DPP-IV, there is concern that inhibition of the cleavage of other endogenous DPP-IV substrates may give rise to undesirable side effects (see, *e.g.*, Chen et al, J Biol Regul Homeost Agents (2004) 18:47-54, the disclosure of which is herein incorporated by reference in its entirety). It therefore would be advantageous to identify a means for achieving increased levels of endogenous GIP activity independently of using a DPP-IV inhibitor or by using substantially lower concentrations of DPP-IV inhibitor than are presently contemplated.

SUMMARY OF THE INVENTION

The present invention relates to the unexpected discovery by Applicant that administration of a GPR119 agonist, such as by oral administration, can act at GPR119 receptor to increase a GIP level in an individual. Applicant has further shown that a GPR119 agonist in combination with a dipeptidyl peptidase IV (DPP-IV) inhibitor can provide an effect in increasing a GIP level in an individual over that provided by the DPP-IV inhibitor alone. The present invention concerns a GPR119 agonist as well as a combination of an amount of a GPR119 agonist with an amount of DPP-IV inhibitor such that the combination provides an effect in increasing a GIP level in an individual over that provided by the amount of the GPR119 agonist or the amount of the DPP-IV inhibitor alone. The present invention further concerns the use of a GPR119 agonist and the use of the combination of a GPR119 agonist with a DPP-IV inhibitor for treating or preventing a condition characterized by low bone mass, such as osteoporosis, and for increasing bone mass in an individual. A GPR119 agonist alone or in combination with a DPP-IV inhibitor is useful for promoting (e.g., increasing) bone formation in an individual. In certain embodiments, the individual is a human.

In a *first aspect*, the present invention features a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising a GPR119 agonist. The present invention additionally features a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a pharmaceutically acceptable carrier. In certain embodiments, the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis.

The present invention features a method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising a GPR119 agonist. The present invention additionally features a method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a pharmaceutically acceptable carrier. In certain embodiments, the individual in need of increased bone mass has a bone mineral density (BMD) greater than 1 (T-score < -1) or greater than or equal to 1.5 (T-score ≤ -1.5), 2 (T-score ≤ -2) or 2.5 (T-score ≤ -2.5) standard deviations below the young adult reference mean. In certain embodiments, the individual in need of increased bone mass is in need of treatment of bone fracture. In certain embodiments, the individual has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic fracture. In certain embodiments, the individual in need of increased bone mass is in need of treatment of a bone disease. In certain embodiments, the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the bone disease is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. In certain embodiments, the individual in need of increased bone mass is in need of enhanced bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis.

In certain embodiments, the GPR119 agonist is a selective GPR119 agonist. In certain embodiments, the GPR119 agonist is selected from the left column of Table D.

In certain embodiments, the administering is oral.

In certain embodiments, the GPR119 agonist is administered in an amount sufficient to increase a GIP level in the individual. In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

In certain embodiments, the individual is a vertebrate. In certain embodiments, the individual is a mammal. In certain embodiments, the individual is a human.

In certain embodiments, the administering is carried out in a single dose.

In certain embodiments, the individual is not a human and the administering is carried out in a single dose.

In certain embodiments, the administering is carried out in multiple doses over a period of greater than 24 days, greater than 36 days, greater than 48 days or greater than 60 days. In certain embodiments, the multiple doses are consecutive daily doses. In certain embodiments, the individual is not a human and the administering is carried out in multiple doses over a period of greater than 24 days, greater than 36 days, greater than 48 days or great than 60 days. In certain embodiments, the individual is not a human and the multiple doses are consecutive daily doses.

In certain embodiments, the individual is a human and the administering is carried out in a single dose.

In certain embodiments, the individual is a human and the administering is carried out in consecutive daily doses over a period of at least 2 days, at least 7 days, at least 14 days, at least 30 days or at least 60 days.

In certain embodiments, the individual is a human and the administering is carried out in multiple doses over a period of greater than 8 weeks, greater than 12 weeks, greater than 16 weeks, greater than 20 weeks, greater than 24 weeks, greater than 28 weeks, greater than 32 weeks or greater than 36 weeks. In certain embodiments, the multiple doses are consecutive daily doses.

In a ***second aspect***, the present invention features use of a GPR119 agonist to treat a condition characterized by low bone mass in the human or animal body by therapy. In certain embodiments, the human or animal body is a human body. In certain embodiments, the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis.

The present invention features use of a GPR119 agonist to increase bone mass in the human or animal body by therapy. In certain embodiments, the human or animal body is a human body. In certain embodiments, the human or animal body has a bone mineral density (BMD) greater than 1 (T-score < -1) or greater than or equal to 1.5 (T-score ≤ -1.5), 2 (T-score ≤ -2) or 2.5 (T-score ≤ -2.5) standard deviations below the young adult reference mean. In certain embodiments, the human or

animal body is in need of treatment of bone fracture. In certain embodiments, the human or animal body has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic fracture. In certain embodiments, the human or animal body is in need of treatment of a bone disease. In certain embodiments, the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the bone disease is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. In certain embodiments, the human or animal body is in need of enhanced bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis.

In certain embodiments, the GPR119 agonist is a selective GPR119 agonist. In certain embodiments, the GPR119 agonist is selected from the left column of Table D.

In certain embodiments, the GPR119 agonist is provided in an amount sufficient to increase a GIP level in the human or animal body. In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

In certain embodiments, the human or animal body is a human body.

In a *third aspect*, the present invention features use of a GPR119 agonist for the manufacture of a medicament for the treatment or prevention of a condition characterized by low bone mass in an individual. In certain embodiments, the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis.

The present invention features use of a GPR119 agonist for the manufacture of a medicament for increasing bone mass in an individual. In certain embodiments, the individual has a bone mineral density (BMD) greater than 1 (T-score < -1) or greater than or equal to 1.5 (T-score ≤ -1.5), 2 (T-score ≤ -2) or 2.5 (T-score ≤ -2.5) standard deviations below the young adult reference mean. In certain embodiments, the individual is in need of treatment of bone fracture. In certain embodiments, the individual has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic fracture. In certain embodiments, the individual is in need of treatment of a bone disease. In certain embodiments, the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions,

curvature of the spine, and loss of height. In certain embodiments, the bone disease is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. In certain embodiments, the individual is in need of enhanced bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis.

In certain embodiments, the GPR119 agonist is a selective GPR119 agonist. In certain embodiments, the GPR119 agonist is selected from the left column of Table D.

In certain embodiments, the GPR119 agonist is provided in an amount sufficient to increase a GIP level in the individual. In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

In certain embodiments, the individual is a vertebrate. In certain embodiments, the individual is a mammal. In certain embodiments, the individual is a human.

In a ***fourth aspect***, the present invention features a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising a GPR119 agonist and a DPP-IV inhibitor. The present invention additionally features a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a DPP-IV inhibitor and a pharmaceutically acceptable carrier. In certain embodiments, the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis.

The present invention features a method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising a GPR119 agonist and a DPP-IV inhibitor. The present invention additionally features a method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a DPP-IV inhibitor and a pharmaceutically acceptable carrier. In certain embodiments, the individual in need of increased bone mass has a bone mineral density (BMD) greater than 1 (T-score < -1) or greater than or equal to 1.5 (T-score ≤ -1.5), 2 (T-score ≤ -2) or 2.5 (T-score ≤ -2.5) standard deviations below the young adult reference mean. In certain embodiments, the individual in need of increased bone mass is in need of treatment of bone fracture. In certain embodiments, the individual has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic fracture. In certain embodiments, the

individual in need of increased bone mass is in need of treatment of a bone disease. In certain embodiments, the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the bone disease is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. In certain embodiments, the individual in need of increased bone mass is in need of enhanced bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis.

In certain embodiments, the GPR119 agonist is a selective GPR119 agonist. In certain embodiments, the GPR119 agonist is selected from the left column of Table D.

In certain embodiments, the DPP-IV inhibitor is a selective DPP-IV inhibitor. In certain embodiments, the DPP-IV inhibitor is selected from the right column of Table D.

In certain embodiments, the GPR119 agonist is selected from the left column of Table D and the DPP-IV inhibitor is selected from the right column of Table D.

In certain embodiments, the administering is oral.

In certain embodiments, the GPR119 agonist or the combination of the GPR119 agonist and the DPP-IV inhibitor is administered in an amount sufficient to increase a GIP level in the individual. In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

In certain embodiments, the individual is a vertebrate. In certain embodiments, the individual is a mammal. In certain embodiments, the individual is a human.

In certain embodiments, the administering is carried out in a single dose.

In certain embodiments, the individual is not a human and the administering is carried out in a single dose.

In certain embodiments, the administering is carried out in multiple doses over a period of greater than 24 days, greater than 36 days, greater than 48 days or greater than 60 days. In certain embodiments, the multiple doses are consecutive daily doses . In certain embodiments, the individual is not a human and the administering is carried out in multiple doses over a period of greater than 24 days, greater than 36 days, greater than 48 days or great than 60 days. In certain embodiments, the individual is not a human and the multiple doses are consecutive daily doses.

In certain embodiments, the individual is a human and the administering is carried out in a single dose.

In certain embodiments, the individual is a human and the administering is carried out in consecutive daily doses over a period of at least 2 days, at least 7 days, at least 14 days, at least 30 days or at least 60 days.

In certain embodiments, the individual is a human and the administering is carried out in multiple doses over a period of greater than 8 weeks, greater than 12 weeks, greater than 16 weeks, greater than 20 weeks, greater than 24 weeks, greater than 28 weeks, greater than 32 weeks or greater than 36 weeks.

In a ***fifth aspect***, the present invention features use of a GPR119 agonist in combination with a DPP-IV inhibitor to treat a condition characterized by low bone mass in the human or animal body by therapy. In certain embodiments, the human or animal body is a human body. In certain embodiments, the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis.

The present invention features use of a GPR119 agonist in combination with a DPP-IV inhibitor to increase bone mass in the human or animal body by therapy. In certain embodiments, the human or animal body is a human body. In certain embodiments, the human or animal body has a bone mineral density (BMD) greater than 1 (T-score < -1) or greater than or equal to 1.5 (T-score ≤ -1.5), 2 (T-score ≤ -2) or 2.5 (T-score ≤ -2.5) standard deviations below the young adult reference mean. In certain embodiments, the human or animal body is in need of treatment of bone fracture. In certain embodiments, the human or animal body has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic fracture. In certain embodiments, the human or animal body is in need of treatment of a bone disease. In certain embodiments, the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the bone disease is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. In certain embodiments, the human or animal body is in need of enhanced bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis.

In certain embodiments, the GPR119 agonist is a selective GPR119 agonist. In certain embodiments, the GPR119 agonist is selected from the left column of Table D.

In certain embodiments, the DPP-IV inhibitor is a selective DPP-IV inhibitor. In certain embodiments, the DPP-IV inhbitor is selected from the right column of Table D.

In certain embodiments, the GPR119 agonist is selected from the left column of Table D and the DPP-IV inhibitor is selected from the right column of Table D.

In certain embodiments, the GPR119 agonist or the combination of a GPR119 agonist and the DPP-IV inhibitor is provided in an amount sufficient to increase a GIP level in the human or animal body. In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

In certain embodiments, the human or animal body is a human body.

In a *sixth aspect*, the present invention features use of a GPR119 agonist in combination with a DPP-IV inhibitor for the manufacture of a medicament for the treatment or prevention of a condition characterized by low bone mass in an individual. In certain embodiments, the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis.

The present invention features use of a GPR119 agonist in combination with a DPP-IV inhibitor for the manufacture of a medicament for increasing bone mass in an individual. In certain embodiments, the individual has a bone mineral density (BMD) greater than 1 (T-score < -1) or greater than or equal to 1.5 (T-score ≤ -1.5), 2 (T-score ≤ -2) or 2.5 (T-score ≤ -2.5) standard deviations below the young adult reference mean. In certain embodiments, the individual is in need of treatment of bone fracture. In certain embodiments, the individual has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic fracture. In certain embodiments, the individual is in need of treatment of a bone disease. In certain embodiments, the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the bone disease is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. In certain embodiments, the individual is in need of enhanced bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis.

In certain embodiments, the GPR119 agonist is a selective GPR119 agonist. In certain embodiments, the GPR119 agonist is selected from the left column of Table D.

In certain embodiments, the DPP-IV inhibitor is a selective DPP-IV inhibitor. In certain embodiments, the DPP-IV inhbitor is selected from the right column of Table D.

In certain embodiments, the GPR119 agonist is selected from the left column of Table D and the DPP-IV inhibitor is selected from the right column of Table D.

In certain embodiments, the GPR119 agonist or the combination of the GPR119 agonist and the DPP-IV inhibitor is provided in an amount sufficient to increase a GIP level in the individual. In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

In certain embodiments, the individual is a vertebrate. In certain embodiments, the individual is a mammal. In certain embodiments, the individual is a human.

In a *seventh aspect*, the invention features a method according to the *first aspect* or to the *fourth aspect*, optionally further comprising the step of identifying the individual as an individual judged by a caregiver to require or benefit from said treating or preventing a condition characterized by low bone mass or from said increasing bone mass, and optionally further comprising the step of identifying achievement of therapeutic efficacy of said administering of said composition or said pharmaceutical composition.

In certain embodiments, the invention features a method of the *first aspect*, further comprising the step of identifying the individual as an individual judged by a caregiver to require or benefit from said treating or preventing a condition characterized by low bone mass or from said increasing bone mass.

In certain embodiments, the invention features a method of the *fourth aspect*, further comprising the step of identifying the individual as an individual judged by a caregiver to require or benefit from said treating or preventing a condition characterized by low bone mass or from said increasing bone mass.

In certain embodiments, the invention features a method of the *first aspect*, further comprising the step of identifying achievement of therapeutic efficacy of said administering of said composition or said pharmaceutical composition.

In certain embodiments, the invention features a method of the *fourth aspect*, further comprising the step of identifying achievement of therapeutic efficacy of said administering of said composition or said pharmaceutical composition.

In certain embodiments, the invention features a method of the *first aspect*, further comprising the step of of identifying the individual as an individual judged by a caregiver to require or benefit from said treating or preventing a condition characterized by low bone mass or from said increasing bone mass, and further comprising the step of identifying achievement of therapeutic efficacy of said administering of said composition or said pharmaceutical composition.

In certain embodiments, the invention features a method of the *fourth aspect*, further comprising the step of of identifying the individual as an individual judged by a caregiver to require or benefit from said treating or preventing a condition characterized by low bone mass or from said increasing bone mass, and further comprising the step of identifying achievement of therapeutic efficacy of said administering of said composition or said pharmaceutical composition.

In certain embodiments wherein the individual is a human, the caregiver is a physician, a nurse or a nurse practioner. In certain embodiments wherein the individual is a non-human vertebrate, and in particular embodiment a non-human mammal, the caregiver is a veterinarian.

In certain embodiments, said identifying achievement of therapeutic efficacy of said administering comprises measuring a level of bone mass in the individual. In certain embodiments, said measuring a level of bone mass comprises measuring the level of bone mass using dual energy X-ray absorptiometry (DXA). In certain embodiments, said measuring a level of bone mass using DXA comprises measuring a T-score using DXA. In certain embodiments, said measuring a T-score using DXA comprises measuring a T-score at the hip using DXA. It is expressly contemplated that said measuring a level of bone mass may comprise measuring a level of bone mass using a technique other than DXA, such as single X-ray absorbtiometry (SXA) [see, e.g., World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis].

In some embodiments, said identifying achievement of therapeutic efficacy of said administering comprises measuring a GIP level in the individual. In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is illustrated in connection with the figures appended hereto in which:

FIG. 1 shows a pharmacodynamic analysis of an effect of administration of GPR119 agonist on blood GIP level in wild-type mice. **A.** A time course analysis carried out using **Compound 1Z** as the GPR119 agonist. **B.** A time course analysis carried out using **Compound 3Z** as the GPR119 agonist. **C.** A dose titration analysis carried out using **Compound 3Z** as the GPR119 agonist.

FIG. 2 shows an effect of administration of GPR119 agonist on blood GIP level in GPR119-deficient (knockout) mice compared to wild-type mice. **A.** The comparison was carried out using **Compound 1Z** as the GPR119 agonist. **B.** The comparison was carried out using **Compound 2Z** as the GPR119 agonist.

FIG. 3 shows an effect of administration of a DPP-IV inhibitor in combination with a GPR119 agonist compared with the DPP-IV inhibitor alone on blood GIP level in wild-type mice. **Compound 1Z** was used as the GPR119 agonist. AR247810 was used as the DPP-IV inhibitor.

DETAILED DESCRIPTION OF THE INVENTION

This invention is concerned with certain compounds, or pharmaceutically acceptable salts thereof, for the treatment or prevention in an individual of a condition characterized by low bone mass, such as osteoporosis. This invention is further concerned with certain compounds, or pharmaceutically acceptable salts thereof, for increasing bone mass in an individual. Applicant has found that administering of a GPR119 agonist to an individual, such as by oral administration, can

increase a GIP level in the individual. A GPR119 agonist is useful for treating or preventing a condition characterized by low bone mass, such as osteoporosis, and for increasing bone mass in an individual.

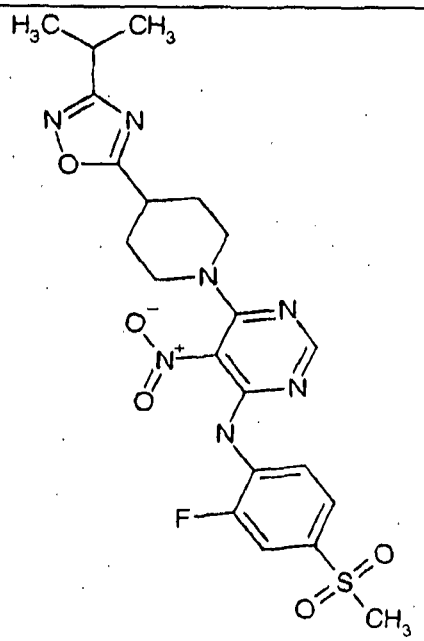
This invention is concerned with the combination of certain compounds, or pharmaceutically acceptable salts thereof, for the treatment or prevention in an individual of a condition characterized by low bone mass, such as osteoporosis. This invention is further concerned with the combination of certain compounds, or pharmaceutically acceptable salts thereof, for increasing bone mass in an individual. An amount of a GPR119 agonist in combination with an amount of a DPP-IV inhibitor can provide an effect in increasing a GIP level in an individual over that provided by the amount of the GPR119 agonist or the amount of the DPP-IV inhibitor alone. The combination of a GPR119 agonist and a DPP-IV inhibitor is useful for the treatment or prevention in an individual of a condition characterized by low bone mass, such as osteoporosis. The combination of a GPR119 agonist and a DPP-IV inhibitor is useful for increasing bone mass in an individual.

By the use of a combination of a GPR119 agonist and a DPP-IV inhibitor in accordance with the present invention, it is possible to treat or prevent a condition characterized by low bone mass more effectively than by use of a GPR119 agonist or a DPP-IV inhibitor alone, thereby reducing the likelihood of unwanted side-effects associated with inhibition of DPP-IV activity. By the use of a combination of a GPR119 agonist and a DPP-IV inhibitor in accordance with the present invention, it is possible to increase bone mass more effectively than by use of a GPR119 agonist or a DPP-IV inhibitor alone, thereby reducing the likelihood of unwanted side-effects associated with inhibition of DPP-IV activity. The present invention provides new, unexpected and advantageous approaches to treating or preventing a condition characterized by low bone mass, such as osteoporosis, and to increasing bone mass in an individual. The present invention additionally provides new, unexpected and advantageous approaches to increasing a GIP level in an individual.

The term "ligand", as used herein, shall mean a molecule (*e.g.*, test compound) that specifically binds to a polypeptide, such as GPR119 or DPP-IV. A ligand may be, for example, a polypeptide, a lipid, a small molecule, an antibody. **Compound 1Z** is an exemplary ligand of GPR119 receptor polypeptide (see, Table E, which sets forth the chemical structure and chemical name of Compound 1Z). Compound 1Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/001267 (published as WO 2004/065380). (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine (*see*, Table E) is an exemplary ligand of GPR119 receptor polypeptide. **Compound 2Z** is an exemplary ligand of GPR119 receptor polypeptide. Compound 2Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/022417 (published as WO 2005/007658). **Compound 3Z** is an exemplary ligand of GPR119 receptor polypeptide. Compound

3Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/022327 (published as WO 2005/007647). An endogenous ligand is a ligand that is an endogenous, natural ligand for a native polypeptide, such as GPR119 or DPP-IV. A ligand may be an "antagonist", "agonist", "partial agonist", or "inverse agonist", or the like. A ligand may be an "inhibitor."

TABLE E

	(2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine

The term "agonist", as used herein, shall mean an agent (*e.g.*, ligand) that by virtue of binding to a GPCR activates the GPCR so as to elicit an intracellular response mediated by the GPCR.

The term "partial agonist", as used herein, shall mean an agent (*e.g.*, ligand) that by virtue of binding to a GPCR activates the GPCR so as to elicit an intracellular response mediated by the GPCR, albeit to a lesser exent or degree than does a full agonist.

The term "antagonist" shall mean an agent (*e.g.*, ligand) that binds, and in particular embodiment binds competitively, to a GPCR at about the same site as an agonist or partial agonist but which does not activate an intracellular response initiated by the active form of the GPCR, and can thereby inhibit the intracellular response by agonist or partial agonist. An anatagonist typically does not diminish the baseline intracellular response in the absence of an agonist or partial agonist.

The term "inverse agonist" shall mean an agent (*e.g.*, ligand) which binds to a GPCR and which inhibits the baseline intracellular response initiated by the active form of the receptor below the normal base level activity which is observed in the absence of an agonist or partial agonist.

The term "GPR119 agonist," as used herein, refers to a compound that binds to GPR119 receptor and acts as an agonist. **Compound 1Z** is an exemplary GPR119 agonist (see, Table E, which sets forth the chemical structure and chemical name of Compound 1Z). Compound 1Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/001267 (published as

WO 2004/065380). (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine is an exemplary GPR119 agonist. **Compound 2Z** is an exemplary GPR119 agonist. Compound 2Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/022417 (published as WO 2005/007658). **Compound 3Z** is an exemplary GPR119 agonist. Compound 3Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/022327 (published as WO 2005/007647).

The term "selective GPR119 agonist," as used herein, refers to a GPR119 agonist having selectivity for GPR119 receptor over one or more related receptors, such as corticotrophin-releasing factor-1 (CRF-1) receptor. **Compound 1Z** is an exemplary selective GPR119 agonist (see, Table E, which sets forth the chemical structure and chemical name of Compound 1Z). Compound 1Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/001267 (published as WO 2004/065380). (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine is an exemplary selective GPR119 agonist. **Compound 2Z** is an exemplary selective GPR119 agonist. Compound 2Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/022417 (published as WO 2005/007658). **Compound 3Z** is an exemplary selective GPR119 agonist. Compound 3Z is identical to a compound disclosed in International Patent Application No. PCT/US2004/022327 (published as WO 2005/007647).

The term "DPP-IV inhibitor," as used herein, refers to a compound that binds to DPP-IV and inhibits DPP-IV dipeptidyl peptidase activity. AR247810 is an exemplary DPP-IV inhibitor.

The term "selective DPP-IV inhibitor," as used herein, refers to a DPP-IV inhibitor having selectivity for DPP-IV over related peptidases, such as one or more of post-proline-cleaving enzyme (PPCE), dipeptidyl peptidase II (DPP-II), dipeptidyl peptidase 8 (DPP-8), and dipeptidyl peptidase 9 (DPP-9). AR247810 is an exemplary selective DPP-IV inhibitor.

The term "blood GIP level" shall mean blood GIP concentration. In certain embodiments, a blood GIP level is a blood total GIP level. In certain embodiments, a blood GIP level is a blood biologically active (bioactive) GIP level. In certain embodiments, bioactive GIP is GIP having agonist activity at GIPR. In certain embodiments, a blood GIP level is a plasma GIP level.

The term "individual," as used herein, refers to a vertebrate, including but not limited to fish (such as commercially farmed fish, pet fish, etc.), amphibians (such as frogs, toads, pet amphibians, etc.), reptiles (such as snakes, lizards, turtles, pet reptiles, etc.), birds (such as chickens, turkeys, pet birds, etc.) and mammals (such as mice, rats, hamsters, rabbits, pigs, dogs, cats, horses, cows, sheep, goats, non-human primates, non-human mammals, pet non-human mammals, humans, etc.). In certain embodiments, the individual is a fish. In certain embodiments, the individual is an amphibian. In certain embodiments, the individual is a reptile. In certain embodiments, the individual is a bird. In certain embodiments, the individual is a turkey. Over the past 25 yr, commercial selection pressure for turkeys with larger breast muscle mass has placed increasing demands on skeletal integrity. The

increased breast muscle mass, however, has not been accompanied by compensatory changes in the skeleton, with the result that the turkey industry has experienced an increase in leg problems. Long bone fracture in young adult male turkeys has been reported. (See, e.g., Crespo et al, Poult Sci (2000) 79:602-608.) In certain embodiments, the individual is a mammal. In certain embodiments, the individual is a mouse, a rat, a hamster, a rabbit, a pig, a dog, a cat, a horse, a cow, a sheep, a goat, a non-human primate or a human (which may be included in embodiments of the invention individually or in any combination). In certain embodiments, the individual is a horse. Performance horses, which are horses involved in activities such as racing, pacing and other competitive events, are susceptible to bone fracture. In certain embodiments, the individual is a dog or a cat. In certain embodiments, the individual is a human companion animal (such as a dog, a cat, etc.), a farm animal (such as a cow, a sheep, a goat, a pig, a chicken, etc.), a sports animal (such as a horse, a dog, etc.), a beast of burden (such as a mule, a camel, etc.) or an exotic animal (such as an animal found in a zoo, etc.), which may be included in embodiments of the invention individually or in any combination. In certain embodiments, the individual is a non-human mammal. In certain embodiments, the individual is a non-human primate (such as a rhesus monkey, a chimpanzee, etc.). In certain embodiments, the individual is a human.

The term "in need of prevention or treatment" as used herein refers to a judgement made by a caregiver (e.g. physician, nurse, nurse practitioner in the case of humans; veterinarian in the case of non-human vertebrates, and in particular embodiment non-human mammals) that an individual requires or will benefit from treatment.

The term "therapeutically effective amount" or "therapeutically effective dose" as used herein refers to the amount of active compound or pharmaceutical agent that elicits the biological or medicinal response in a tissue, system, animal, individual or human that is being sought by a researcher, veterinarian, medical doctor or other clinician, which includes one or more of the following:

(1) Preventing the disease; for example, preventing a disease, condition or disorder in an individual that may be predisposed to the disease, condition or disorder but does not yet experience or display the pathology or symptomatology of the disease,

(2) Inhibiting the disease; for example, inhibiting a disease, condition or disorder in an individual that is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (i.e., arresting further development of the pathology and/or symptomatology), and

(3) Ameliorating the disease; for example, ameliorating a disease, condition or disorder in an individual that is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (i.e., reversing the pathology and/or symptomatology).

The term "therapeutic efficacy" as used herein refers to elicitation of the biological or medicinal response in a tissue, system, animal, individual or human that is being sought by a researcher, veterinarian, medical doctor or other clinician, which includes one or more of the following:

(1) Preventing the disease; for example, preventing a disease, condition or disorder in an individual that may be predisposed to the disease, condition or disorder but does not yet experience or display the pathology or symptomatology of the disease,

(2) Inhibiting the disease; for example, inhibiting a disease, condition or disorder in an individual that is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (i.e., arresting further development of the pathology and/or symptomatology), and

(3) Ameliorating the disease; for example, ameliorating a disease, condition or disorder in an individual that is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (i.e., reversing the pathology and/or symptomatology).

The term "amount that is effective to prevent" refers to that amount of drug that will prevent or reduce the risk of occurrence of the biological or medical event that is sought to be prevented. In many instances, the amount that is effective to prevent is the same as the therapeutically effective amount.

The term "composition" shall mean a material comprising at least one component.

The term "active ingredient" shall mean any component that provides pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease.

The term "pharmaceutical composition" shall mean a composition comprising at least one active ingredient, whereby the composition is amenable to investigation and treatment in a mammal.

By "pharmaceutically acceptable" it is meant that the carrier, vehicle, diluent, excipients, and/or salt must be compatible with the other ingredients of the formulation, and not deleterious to the recipient thereof.

The term "dosage form" shall mean the physical form in which a drug is produced and dispensed, such as a tablet, capsule, or an injectable.

By "bone" is intended the dense, semi-rigid, porous, calcified connective tissue forming the major portion of the skeleton of most vertebrates, comprising a dense organic matrix and an inorganic, mineral component. Bone is any of numerous anatomically distinct structures making up the skeleton of a vertebrate.

The terms "bone mass" and "bone mineral density (BMD)" are used interchangeably herein. BMD in humans is usually measured by a standard radiographic technique, dual energy X-ray absorptiometry (DXA). Of the many techniques developed to assess BMD, DXA is the most highly developed technically and the most thoroughly validated biologically. DXA technology, with suitably adapted software, can also be used to reliably assess BMD in animal studies. DXA is used in the diagnosis of osteoporosis, prognosis (fracture prediction), monitoring the natural history of the disorder, and assessing response to treatment.

The term "low bone mass" as used herein refers to any decrease or reduction in bone mineral density (BMD) in an individual, and includes both osteoporosis and osteopenia as defined in proposals by the World Health Organization (WHO). The WHO has defined normal as a value of

BMD within one standard deviation of the young adult reference mean (T-score ≥ -1). The WHO has defined osteopenia as a value of BMD more than 1 standard deviation below the young adult mean, but less than 2.5 standard deviations below this value (T-score < -1 and > -2.5). The WHO has characterized osteoporosis as a more severe form of osteopenia, and has defined it by value of BMD 2.5 standard deviations or more blow the young adult mean (T-score ≤ -2.5). (See, e.g., World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis, the disclosure of which is herein incorporated by reference in its entirety.) More commonly, osteopenia is defined as a T-score of less than -1 and greater than -2, and osteoporosis is defined as a T-score of less than or equal to -2. In certain embodiments of the present invention, the T-score is measured at the hip with DXA.

The term "osteoporosis" as used herein is defined by a value of BMD 2 standard deviations or more below the young adult reference mean (T-score ≤ -2) or refers to a diagnosis made by a caregiver (e.g. physician, nurse, nurse practitioner in the case of humans; veterinarian in the case of non-human vertebrates).

Osteoporosis can be classified as either primary or secondary. (See, e.g., World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis.) As used herein, the term "osteoporosis" encompasses primary osteoporosis and secondary osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis.

"Primary osteoporosis" as used herein is associated with menopause (natural, premature, or surgical), aging, or both. It shall be understood that in the present invention, primary osteoporosis associated with menopause (natural, premature, or surgical), primary osteoporosis associated with aging, and primary osteoporosis associated with menopause and aging can be included in embodiments individually or in any combination.

"Secondary osteoporosis" as used herein refers to osteoporosis which is associated not with menopause or aging but rather with medical conditions or with the use of medications or drugs. An increased risk of osteoporosis is associated with a host of medical conditions, including but not limited to endocrine and metabolic disorders, and malignant disease, and with the use of certain medications and drugs, examples of which are well known to those skilled in the art (see, *e.g.*, World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis; Williams Textbook of Endocrinology, 10th Edition; the disclosure of which is herein incorporated by reference in its entirety.) Secondary osteoporosis can also be associated with immobilization. A diagnosis of osteoporosis secondary to a medical condition, to use of a medication or drug, or to immobilization can be made by a caregiver (e.g. physician, nurse, nurse practitioner in the case of humans; veterinarian in the case of non-human vertebrates).

By "bone fracture" is intended a complete or incomplete break, rupture or crack of a bone. Diagnosis of fractures normally depends upon clinical examination and radiological findings. In the

invention, bone fractures include, but are not limited to, traumatic fractures, long-term fractures, and pathological fractures.

"Traumatic fracture" as used herein shall refer to an immediate fracture which involves a supraliminal trauma with a degree of local violence that exceeds the natural elasticity of the bone. It can be accompanied by simultaneous injury to the soft tissues and very often the skin. A traumatic fracture can be closed (the adjacent soft tissue can be injured but the covering soft parts are largely preserved). A traumatic fracture can be open (the broken ends of the bone are freed by extensive soft tissue injury so that pathogens from outside can enter the wound directly).

"Long-term fracture" as used herein shall refer to a chronic fracture, fatigue fracture, stress fracture or spontaneous fracture type I.

"Pathological fracture" as used herein shall refer to a spontaneous fracture type II. A pathological fracture arises spontaneously, without adequate trauma to account for it. The bone may have been previously damaged, either by a systemic disease (e.g., osteoporosis, osteodystrophy, or Paget's osteitis deformans) or by a local bone lesion (e.g., metastasis, radioosteonecrosis, or bone tumor). See, Adler, Claus-Peter, BONE DISEASES, p. 114 (Springer-Verlag, Germany 2000).

Fractures also include, but are not limited no, oblique torsion fracture, transverse fracture, comminuted fracture, compression fracture, rib fractures, creeping fracture, and fractured femoral neck (Adler, Claus-Peter, BONE DISEASES, Springer-Verlag, Germany (2000)).

As used herein, the term "condition characterized by low bone mass" includes but is not limited to osteopenia, osteoporosis, primary osteoporosis, secondary osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, curvature of the spine and loss of height. In certain embodiments, secondary osteoporosis is associated with a medical condition. In certain embodiments, secondary osteoporosis is associated with use of a medication or drug. In certain embodiments, secondary osteoporosis is associated with immobilization. Conditions characterized by low bone mass include but are not limited to Paget's disease, bone loss due to metastatic cancer, and osteolytic lesions such as those caused by neoplastic disease, radiotherapy, or chemotherapy. Conditions characterized by low bone mass also include but are not limited to long-term complications of osteoporosis such as curvature of the spine, loss of height and prosthetic surgery. It shall be understood that in the present invention, conditions characterized by low bone mass can be included in embodiments individually or in any combination. (See, e.g., World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis; Williams Textbook of Endocrinology, 10th Edition, Larsen et al, Eds. (2002), W.B. Saunders Company; and Endocrinology and Metabolism, 4th Edition, Felig et al, Eds. (2001), McGraw-Hill Book Company; the disclosure of each of which is herein incorporated by reference in its entirety.)

As used herein, "bone disease" refers to a disorder or condition relating to abnormality of the bone. Bone diseases that can be treated according to the invention, by increasing bone mass or bone

growth, include but are not limited to osteopenia, osteoporosis, primary osteoporosis, secondary osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, curvature of the spine, and loss of height. In certain embodiments, secondary osteoporosis is associated with a medical conditions. In certain embodiments, secondary osteoporosis is associated with the use of a medication or drug. In certain embodiments, secondary osteoporosis is associated with immobilization. Bone diseases that can be treated according to the invention, by increasing bone mass or bone growth, also include but are not limited to Paget's disease and bone loss due to metastatic cancer. Destructive bone disorders that can be treated according to the invention, by increasing bone mass or growth, include but are not limited to osteoporosis, osteoarthritis, and osteolytic lesions such as those caused by neoplastic disease, radiotherapy, or chemotherapy. It shall be understood that in the present invention, bone diseases that can be treated according to the invention, by increasing bone mass or growth, can be included in embodiments individually or in any combination. (See, e.g., World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis; Williams Textbook of Endocrinology, 10th Edition, Larsen et al, Eds. (2002), W.B. Saunders Company; and Endocrinology and Metabolism, 4th Edition, Felig et al, Eds. (2001), McGraw-Hill Book Company; the disclosure of each of which is herein incorporated by reference in its entirety.)

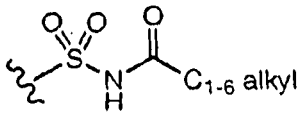
The present invention also relates to the other conditions that derive benefit from treatment according to the invention, by increasing bone mass or bone growth, including but not limited to enhanced bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth and increased bone synostosis.

Chemical Group, Moiety or Radical

The term "**C_{1-5} acyl**" denotes a C_{1-5} alkyl radical attached to a carbonyl wherein the definition of alkyl has the same definition as described herein; some examples include but not limited to, acetyl, propionyl, n-butanoyl, *iso*-butanoyl, sec-butanoyl, t-butanoyl (i.e., pivaloyl), pentanoyl and the like.

The term "**C_{1-5} acyloxy**" denotes an acyl radical attached to an oxygen atom wherein acyl has the same definition has described herein; some examples include but not limited to acetyloxy, propionyloxy, butanoyloxy, *iso*-butanoyloxy, sec-butanoyloxy, t-butanoyloxy and the like.

The term "**C_{1-6} acylsulfonamide**" refers to a C_{1-6} acyl attached directly to the nitrogen of the sulfonamide, wherein the definitions for C_{1-6} acyl and sulfonamide have the same meaning as described herein, and a C_{1-6} acylsulfonamide can be represented by the following formula:



Some embodiments of the present invention are when acylsulfonamide is a C_{1-5} acylsulfonamide, some embodiments are C_{1-4} acylsulfonamide, some embodiments are C_{1-3} acylsulfonamide, and some

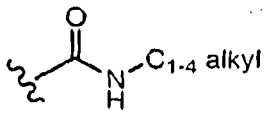
embodiments are C_{1-2} acylsulfonamide. Examples of an acylsulfonamide include, but not limited to, acetylsulfamoyl [$-S(=O)_2NHC(=O)Me$], propionylsulfamoyl [$-S(=O)_2NHC(=O)Et$], isobutyrylsulfamoyl, butyrylsulfamoyl, 2-methyl-butyrylsulfamoyl, 3-methyl-butyrylsulfamoyl, 2,2-dimethyl-propionylsulfamoyl, pentanoylsulfamoyl, 2-methyl-pentanoylsulfamoyl, 3-methyl-pentanoylsulfamoyl, 4-methyl-pentanoylsulfamoyl, and the like.

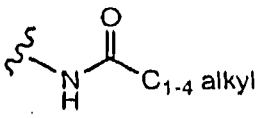
The term "**C_{2-6} alkenyl**" denotes a radical containing 2 to 6 carbons wherein at least one carbon-carbon double bond is present, some embodiments are 2 to 4 carbons, some embodiments are 2 to 3 carbons, and some embodiments have 2 carbons. Both *E* and *Z* isomers are embraced by the term "**alkenyl.**" Furthermore, the term "**alkenyl**" includes di- and tri-alkenyls. Accordingly, if more than one double bond is present then the bonds may be all *E* or *Z* or a mixtures of *E* and *Z*. Examples of an alkenyl include vinyl, allyl, 2-butenyl, 3-butenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexanyl, 2,4-hexadienyl and the like.

The term "**C_{1-4} alkoxy**" as used herein denotes a radical alkyl, as defined herein, attached directly to an oxygen atom. Examples include methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, t-butoxy, iso-butoxy, sec-butoxy and the like.

The term "**C_{1-8} alkyl**" denotes a straight or branched carbon radical containing 1 to 8 carbons, some embodiments are 1 to 6 carbons, some embodiments are 1 to 3 carbons, and some embodiments are 1 or 2 carbons. Examples of an alkyl include, but not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, t-butyl, pentyl, iso-pentyl, t-pentyl, neo-pentyl, 1-methylbutyl [i.e., $-CH(CH_3)CH_2CH_2CH_3$], 2-methylbutyl [i.e., $-CH_2CH(CH_3)CH_2CH_3$], n-hexyl and the like.

The term "**C_{1-4} alkylcarboxamido**" or "**C_{1-4} alkylcarboxamide**" denotes a single C_{1-4} alkyl group attached to the nitrogen of an amide group, wherein alkyl has the same definition as found herein. The C_{1-5} alkylcarboxamido may be represented by the following:





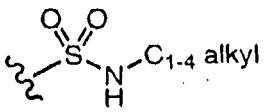
Examples include, but not limited to, *N*-methylcarboxamide, *N*-ethylcarboxamide, *N*-n-propylcarboxamide, *N*-iso-propylcarboxamide, *N*-n-butylcarboxamide, *N*-sec-butylcarboxamide, *N*-iso-butylcarboxamide, *N*-t-butylcarboxamide and the like.

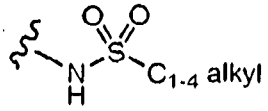
The term "**C_{1-3} alkylene**" refers to a C_{1-3} divalent straight carbon group. In some embodiments C_{1-3} alkylene refers to, for example, $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, and the like. In some embodiments, C_{1-3} alkylene refers to -CH-, $-CHCH_2-$, $-CHCH_2CH_2-$, and the like wherein these examples relate generally to "A".

The term "**C_{1-4} alkylsulfinyl**" denotes a C_{1-4} alkyl radical attached to a sulfoxide radical of the formula: -S(O)- wherein the alkyl radical has the same definition as described herein. Examples

include, but not limited to, methylsulfinyl, ethylsulfinyl, n-propylsulfinyl, iso-propylsulfinyl, n-butylsulfinyl, sec-butylsulfinyl, iso-butylsulfinyl, t-butyl, and the like.

The term "**C_{1-4} alkylsulfonamide**" refers to the groups



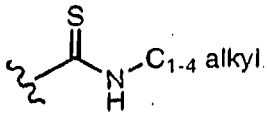


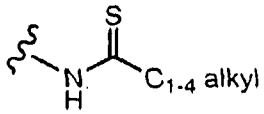
wherein C_{1-4} alkyl has the same definition as described herein.

The term "**C_{1-4} alkylsulfonyl**" denotes a C_{1-4} alkyl radical attached to a sulfone radical of the formula: $-S(O)_2-$ wherein the alkyl radical has the same definition as described herein. Examples include, but not limited to, methylsulfonyl, ethylsulfonyl, n-propylsulfonyl, iso-propylsulfonyl, n-butylsulfonyl, sec-butylsulfonyl, iso-butylsulfonyl, t-butyl, and the like.

The term "**C_{1-4} alkylthio**" denotes a C_{1-4} alkyl radical attached to a sulfide of the formula: -S- wherein the alkyl radical has the same definition as described herein. Examples include, but not limited to, methylsulfanyl (i.e., CH_3S-), ethylsulfanyl, n-propylsulfanyl, iso-propylsulfanyl, n-butylsulfanyl, sec-butylsulfanyl, iso-butylsulfanyl, t-butyl, and the like.

The term "**C_{1-4} alkylthiocarboxamide**" denotes a thioamide of the following formulae:





wherein C_{1-4} alkyl has the same definition as described herein.

The term "**C_{1-4} alkylthioureyl**" denotes the group of the formula: -NC(S)N- wherein one are both of the nitrogens are substituted with the same or different C_{1-4} alkyl groups and alkyl has the same definition as described herein. Examples of an alkylthioureyl include, but not limited to, $CH_3NHC(S)NH-$, $NH_2C(S)NCH_3-$, $(CH_3)_2N(S)NH-$, $(CH_3)_2N(S)NH-$, $(CH_3)_2N(S)NCH_3-$, $CH_3CH_2NHC(S)NH-$, $CH_3CH_2NHC(S)NCH_3-$, and the like.

The term "**C_{1-4} alkylureyl**" denotes the group of the formula: -NC(O)N- wherein one are both of the nitrogens are substituted with the same or different C_{1-4} alkyl group wherein alkyl has the same definition as described herein. Examples of an alkylureyl include, but not limited to, $CH_3NHC(O)NH-$, $NH_2C(O)NCH_3-$, $(CH_3)_2N(O)NH-$, $(CH_3)_2N(O)NH-$, $(CH_3)_2N(O)NCH_3-$, $CH_3CH_2NHC(O)NH-$, $CH_3CH_2NHC(O)NCH_3-$, and the like.

The term "**C_{2-6} alkynyl**" denotes a radical containing 2 to 6 carbons and at least one carbon-carbon triple bond, some embodiments are 2 to 4 carbons, some embodiments are 2 to 3 carbons, and some embodiments have 2 carbons. Examples of an alkynyl include, but not limited to, ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, 1-pentynyl, 2-pentynyl, 3-pentynyl, 4-pentynyl, 1-hexynyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, 5-hexynyl and the like. The term "**alkynyl**" includes di- and tri-ynes.

The term "**amino**" denotes the group $-NH_2$.

The term "**C_{1-4} alkylamino**" denotes one alkyl radical attached to an amino radical wherein the alkyl radical has the same meaning as described herein. Some examples include, but not limited to, methylamino, ethylamino, n-propylamino, iso-propylamino, n-butylamino, sec-butylamino, iso-butylamino, t-butylamino, and the like. Some embodiments are "**C_{1-2} alkylamino**."

The term "**aryl**" denotes an aromatic ring radical containing 6 to 10 ring carbons. Examples include phenyl and naphthyl.

The term "**arylalkyl**" defines a C_1-C_4 alkylene, such as $-CH_2-$, $-CH_2CH_2-$ and the like, which is further substituted with an aryl group. Examples of an "arylalkyl" include benzyl, phenethylene and the like.

The term "**arylcarboxamido**" denotes a single aryl group attached to the nitrogen of an amide group, wherein aryl has the same definition as found herein. The example is *N*-phenylcarboxamide.

The term "**arylureyl**" denotes the group -NC(O)N- where one of the nitrogens are substituted with an aryl.

The term "**benzyl**" denotes the group $-CH_2C_6H_5$.

The term "**carbo-C_{1-6}-alkoxy**" refers to a C_{1-6} alkyl ester of a carboxylic acid, wherein the alkyl group is as defined herein. In some embodiments, the carbo-C_{1-6}-alkoxy group is bonded to a nitrogen atom and together form a carbamate group (e.g., N-COO-C_{1-6}-alkyl). In some embodiments, the carbo-C_{1-6}-alkoxy group is an ester (e.g., -COO-C_{1-6}-alkyl). Examples include, but not limited to, carbomethoxy, carboethoxy, carbopropoxy, carboisopropoxy, carbobutoxy, carbo-sec-butoxy, carbo-iso-butoxy, carbo-t-butoxy, carbo-n-pentoxy, carbo-iso-pentoxy, carbo-t-pentoxy, carbo-neo-pentoxy, carbo-n-hexyloxy, and the like.

The term "**carboxamide**" refers to the group $-CONH_2$.

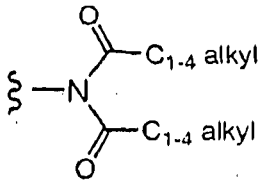
The term "**carboxy**" or "**carboxyl**" denotes the group $-CO_2H$; also referred to as a carboxylic acid group.

The term "**cyano**" denotes the group –CN.

The term "**C_{3-7} cycloalkenyl**" denotes a non-aromatic ring radical containing 3 to 6 ring carbons and at least one double bond; some embodiments contain 3 to 5 carbons; some embodiments contain 3 to 4 carbons. Examples include cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclopentenyl, cyclohexenyl, and the like.

The term "**C_{3-7} cycloalkyl**" denotes a saturated ring radical containing 3 to 6 carbons; some embodiments contain 3 to 5 carbons; some embodiments contain 3 to 4 carbons. Examples include cyclopropyl, cyclobutyl, cyclopentyl, cyclopenyl, cyclohexyl, cycloheptyl and the like.

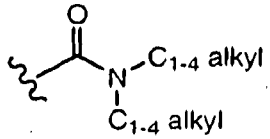
The term "**C_{4-8} diacylamino**" denotes an amino group bonded with two acyl groups defined herein wherein the acyl groups may be the same or different, such as:

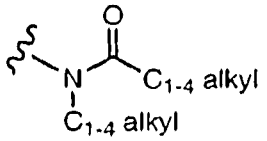


Examples of C_{4-8} diacylamino groups include, but limited to, diacetylamino, dipropionylamino, acetylpropionylamino and the like.

The term "**C_{2-6} dialkylamino**" denotes an amino substituted with two of the same or different alkyl radicals wherein alkyl radical has the same definition as described herein. Some examples include, but not limited to, dimethylamino, methylethylamino, diethylamino, methylpropylamino, methylisopropylamino, ethylpropylamino, ethylisopropylamino, dipropylamino, propylisopropylamino and the like. Some embodiments are "**C_{2-4} dialkylamino.**"

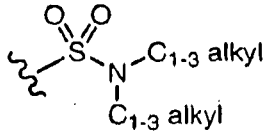
The term "**C_{1-4} dialkylcarboxamido**" or "**C_{1-4} dialkylcarboxamide**"denotes two alkyl radicals, that are the same or different, attached to an amide group, wherein alkyl has the same definition as described herein. A C_{1-4} dialkylcarboxamido may be represented by the following groups:

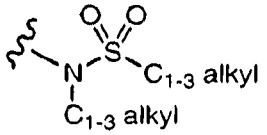




wherein C_{1-4} has the same definition as described herein. Examples of a dialkylcarboxamide include, but not limited to, *N*,*N*-dimethylcarboxamide, *N*-methyl-*N*-ethylcarboxamide, *N*,*N*-diethylcarboxamide, *N*-methyl-*N*-isopropylcarboxamide, and the like.

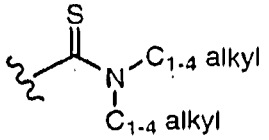
The term "**C_{2-6} dialkylsulfonamide**" refers to one of the following groups shown below:

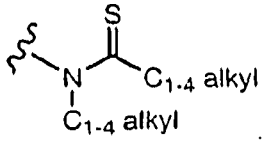




wherein C_{1-3} has the same definition as described herein, for example but not limited to, methyl, ethyl, n-propyl, isopropyl, and the like.

The term "**C_{2-6} dialkylthiocarboxamido**" or "**C_{2-6} dialkylthiocarboxamide**"denotes two alkyl radicals, that are the same or different, attached to a thioamide group, wherein alkyl has the same definition as described herein. A C_{1-4} dialkylthiocarboxamido may be represented by the following groups:

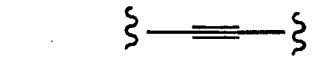




Examples of a dialkylthiocarboxamide include, but not limited to, *N*,*N*-dimethylthiocarboxamide, *N*-methyl-*N*-ethylthiocarboxamide and the like.

The term "**C_{2-6} dialkylsulfonylamino**" refers to an amino group bonded with two C_{1-3} alkylsulfonyl groups as defined herein.

The term "**ethynylene**" refers to the carbon-carbon triple bond group as represented below:



The term "**formyl**" refers to the group –CHO.

The term "**C_{1-4} haloalkoxy**" denotes a haloalkyl, as defined herein, which is directly attached to an oxygen atom. Examples include, but not limited to, difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, pentafluoroethoxy and the like.

The term "**C_{1-4} haloalkyl**" denotes an C_{1-4} alkyl group, defined herein, wherein the alkyl is substituted with one halogen up to fully substituted and a fully substituted C_{1-4} haloalkyl can be represented by the formula C_nL_{2n+1} wherein L is a halogen and "n" is 1, 2, 3 or 4; when more than one halogen is present then they may be the same or different and selected from the group consisting of F, Cl, Br and I, in particular embodiment F. Examples of C_{1-4} haloalkyl groups include, but not limited to, fluoromethyl, difluoromethyl, trifluoromethyl, chlorodifluoromethyl, 2,2,2-trifluoroethyl, pentafluoroethyl and the like.

The term "**C_{1-4} haloalkylcarboxamide**" denotes an alkylcarboxamide group, defined herein, wherein the alkyl is substituted with one halogen up to fully substituted represented by the formula C_nL_{2n+1} wherein L is a halogen and "n" is 1, 2, 3 or 4. When more than one halogen is present they may be the same or different and selected from the group consisting of F, Cl, Br and I, in particular embodiment F.

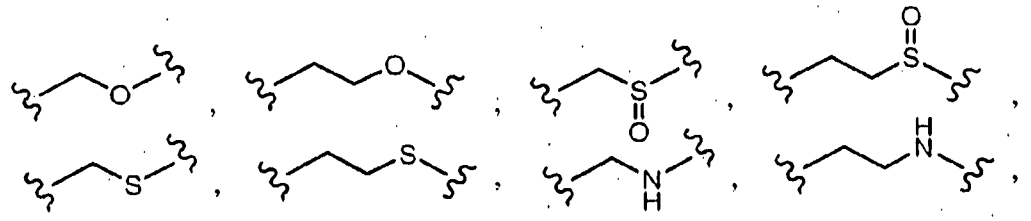
The term "**C_{1-4} haloalkylsulfinyl**" denotes a haloalkyl radical attached to a sulfoxide group of the formula: -S(O)- wherein the haloalkyl radical has the same definition as described herein. Examples include, but not limited to, trifluoromethylsulfinyl, 2,2,2-trifluoroethylsulfinyl, 2,2-difluoroethylsulfinyl and the like.

The term "**C_{1-4} haloalkylsulfonyl**" denotes a haloalkyl radical attached to a sulfone group of the formula: -$S(O)_2$- wherein haloalkyl has the same definition as described herein. Examples include, but not limited to, trifluoromethylsulfonyl, 2,2,2-trifluoroethylsulfonyl, 2,2-difluoroethylsulfonyl and the like.

The term "**C_{1-4} haloalkylthio**" denotes a haloalkyl radicaol directly attached to a sulfur wherein the haloalkyl has the same meaning as described herein. Examples include, but not limited to, trifluoromethylthio (i.e., CF_3S-), 1,1-difluoroethylthio, 2,2,2-trifluoroethylthio and the like.

The term "**halogen**" or "**halo**" denotes to a fluoro, chloro, bromo or iodo group.

The term "**C_{1-2} heteroalkylene**" refers to a C_{1-2} alkylene bonded to a heteroatom selected from O, S, S(O), $S(O)_2$ and NH. Some represented examples include, but not limited to, the groups of the following formulae:

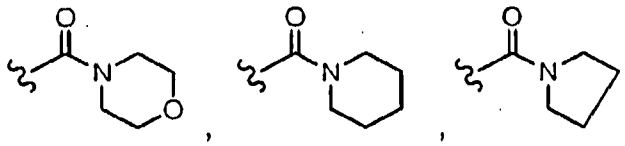


and the like.

The term "**heteroaryl**" denotes an aromatic ring system that may be a single ring, two fused rings or three fused rings wherein at least one ring carbon is replaced with a heteroatom selected from, but not limited to, the group consisting of O, S and N wherein the N can be optionally substituted with H, C_{1-4} acyl or C_{1-4} alkyl. Examples of heteroaryl groups include, but not limited to, pyridyl, benzofuranyl, pyrazinyl, pyridazinyl, pyrimidinyl, triazinyl, quinoline, benzoxazole, benzothiazole, 1*H*-benzimidazole, isoquinoline, quinazoline, quinoxaline and the like. In some embodiments, the heteroaryl atom is O, S, NH, examples include, but not limited to, pyrrole, indole, and the like.

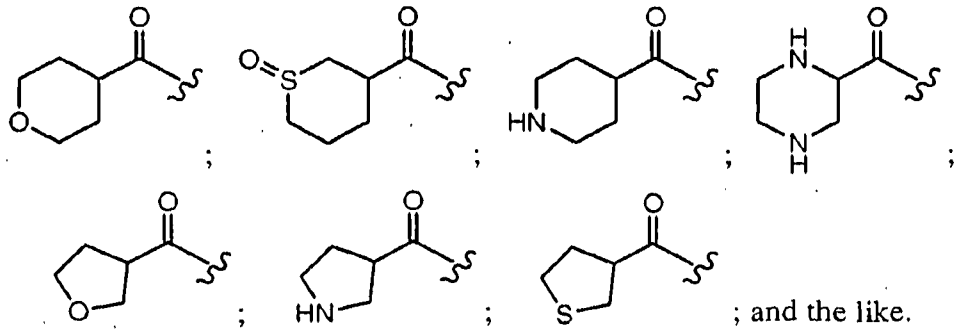
The term "**heterocyclic**" denotes a non-aromatic carbon ring (i.e., cycloalkyl or cycloalkenyl as defined herein) wherein one, two or three ring carbons are replaced by a heteroatom selected from, but not limited to, the group consisting of O, S, N, wherein the N can be optionally substituted with H, C_{1-4} acyl or C_{1-4} alkyl, and ring carbon atoms optionally substituted with oxo or a thiooxo thus forming a carbonyl or thiocarbonyl group. The heterocyclic group is a 3-, 4-, 5-, 6- or 7-membered containing ring. Examples of a heterocyclic group include but not limited to aziridin-1-yl, aziridin-2-yl, azetidin-1-yl, azetidin-2-yl, azetidin-3-yl, piperidin-1-yl, piperidin-4-yl, morpholin-4-yl, piperzin-1-yl, piperzin-4-yl, pyrrolidin-1-yl, pyrrolidin-3-yl, [1,3]-dioxolan-2-yl and the like.

The term "**heterocyclic-carbonyl**" denotes a heterocyclic group, as defined herein, directly bonded to the carbon of a carbonyl group (i.e., C=O). In some embodiments, a ring nitrogen of the heterocyclic group is bonded to the carbonyl group forming an amide. Examples include, but not limited to,



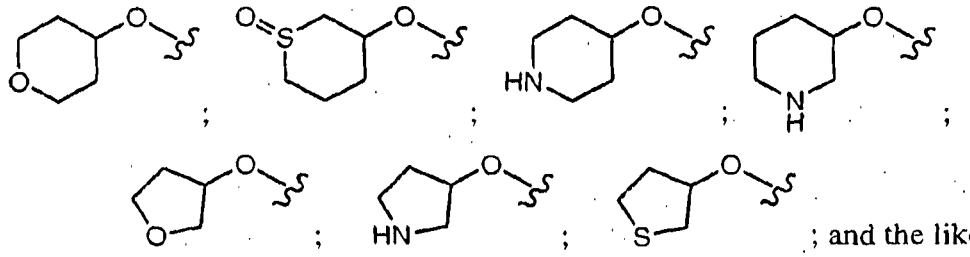
and the like.

In some embodiments, a ring carbon is bonded to the carbonyl group forming a ketone group. Examples include, but not limited to,



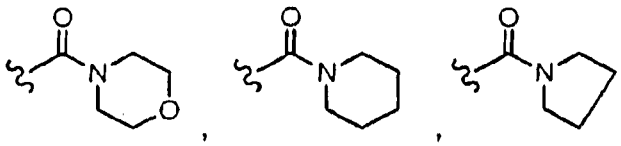
; and the like.

The term "**heterocyclic-oxy**" refers to a heterocyclic group, as defined herein, that is directly bonded to an oxygen atom. Examples include the following:



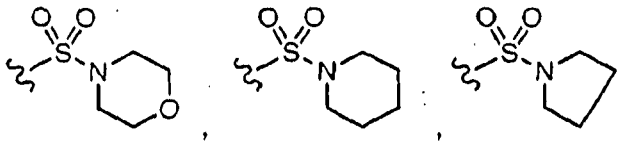
; and the like.

The term "**heterocycliccarboxamido**" denotes a heterocyclic group, as defined herein, with a ring nitrogen where the ring nitrogen is bonded directly to the carbonyl forming an amide. Examples include, but not limited to,



and the like.

The term "**heterocyclicsulfonyl**" denotes a heterocyclic group, as defined herein, with a ring nitrogen where the ring nitrogen is bonded directly to an SO_2 group forming an sulfonamide. Examples include, but not limited to,



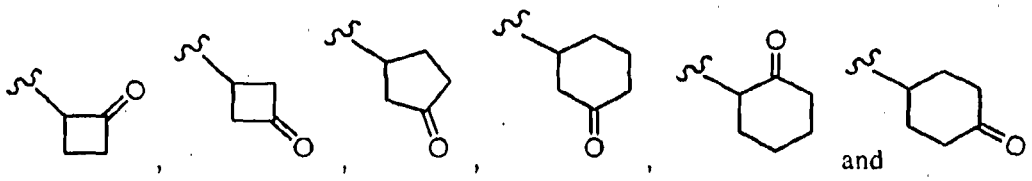
and the like.

The term "**hydroxyl**" refers to the group -OH.

The term "**hydroxylamino**" refers to the group -NHOH.

The term "**nitro**" refers to the group $-NO_2$.

The term "**C_{4-7} oxo-cycloalkyl**" refers to a C_{4-7} cycloalkyl, as defined herein, wherein one of the ring carbons is replaced with a carbonyl. Examples of C_{4-7} oxo-cycloalkyl include, but are not limited to, 2-oxo-cyclobutyl, 3-oxo-cyclobutyl, 3-oxo-cyclopentyl, 4-oxo-cyclohexyl, and the like and represented by the following structures respectively:



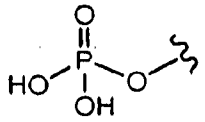
and

The term "**perfluoroalkyl**" denotes the group of the formula $-C_nF_{2n+1}$; stated differently, a perfluoroalkyl is an alkyl as defined herein wherein the alkyl is fully substituted with fluorine atoms and is therefore considered a subset of haloalkyl. Examples of perfluoroalkyls include CF_3, CF_2CF_3, $CF_2CF_2CF_3$, $CF(CF_3)_2$, $CF_2CF_2CF_2CF_3$, $CF_2CF(CF_3)_2$, $CF(CF_3)CF_2CF_3$ and the like.

The term "**phenoxy**" refers to the group C_6H_5O-.

The term "**phenyl**" refers to the group C_6H_5-.

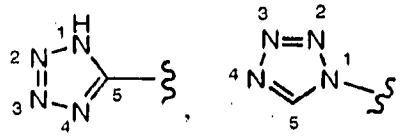
The term "**phosphonooxy**" refers to a group with the following chemical structure:



The term "**sulfonamide**" refers to the group $-SO_2NH_2$.

The term "**sulfonic acid**" refers to the group $-SO_3H$.

The term "**tetrazolyl**" refers to the five membered heteroaryl of the following formulae:



In some embodiments, the tetrazolyl group is further substituted at either the 1 or 5 position resepectively with a group selected from the group consisting of C_{1-3} alkyl, C_{1-3} haloalkyl and C_{1-3} alkoxy.

The term "**thiol**" denotes the group –SH.

The term "endogenous" shall mean a material that an individual (for example, and not limitation, a human) naturally produces. By contrast, "non-endogenous" shall mean that which is not naturally produced by an individual (for example, and not limitation, a human).

The term "host cell" shall mean a cell capable of having a vector incorporated therein. In the present context, the vector will typically contain nucleic acid encoding a GPCR or GPCR fusion protein in operable conncection with a suitable promoter sequence to permit expression of the GPCR or GPCR fusion protein to occur. In particular embodiment, the host cell is a eukaryotic host cell. In certain embodiments, the eukaryotic host cell is a mammalian host cell. In certain embodiments, the eukaryotic host cell is a yeast host cell. In certain embodiments, the eukaryotic host cell is a melanophore host cell.

The term "contact" or "contacting" shall mean bringing at least two moieties together.

The terms "modulate" or "modify" shall be taken to refer to an increase or decrease in the amount, quality, or effect of a particular activity, function or molecule. By way of illustration and not limitation, agonists, partial agonists, inverse agonists, and antagonists of a G protein-coupled receptor are modulators of the receptor.

The term "small molecule" shall be taken to mean a compound having a molecular weight of less than about 10,000 grams per mole, including a peptide, peptidomimetic, amino acid, amino acid analogue, polynucleotide, polynucleotide analogue, nucleotide, nucleotide analogue, organic compound or inorganic compound (i.e. including a heterorganic compound or organometallic compound), and salts, esters and other pharmaceutically acceptable forms thereof. In certain embodiments, small molecules are organic or inorganic compounds having a molecular weight of less than about 5,000 grams per mole. In certain embodiments, small molecules are organic or inorganic compounds having molecular weight of less than about 1,000 grams per mole. In certain

embodiments, small molecules are organic or inorganic compounds having a molecular weight of less than about 800 grams per mole. In certain embodiments, small molecules are organic or inorganic compounds having a molecular weight of less than about 600 grams per mole. In certain embodiments, small molecules are organic or inorganic compounds having a molecular weight of less than about 500 grams per mole.

Amino acid abbreviations used herein are set out in **Table F**:

TABLE F

ALANINE	ALA	A
ARGININE	ARG	R
ASPARAGINE	ASN	N
ASPARTIC ACID	ASP	D
CYSTEINE	CYS	C
GLUTAMIC ACID	GLU	E
GLUTAMINE	GLN	Q
GLYCINE	GLY	G
HISTIDINE	HIS	H
ISOLEUCINE	ILE	I
LEUCINE	LEU	L
LYSINE	LYS	K
METHIONINE	MET	M
PHENYLALANINE	PHE	F
PROLINE	PRO	P
SERINE	SER	S
THREONINE	THR	T
TRYPTOPHAN	TRP	W
TYROSINE	TYR	Y
VALINE	VAL	V

The term "polypeptide" shall refer to a polymer of amino acids without regard to the length of the polymer. Thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide. This term also does not specify or exclude post-expression modifications of polypeptides. For example, polypeptides that include the covalent attachment of glycosyl groups,

acetyl groups, phosphate groups, lipid groups and the like are expressly encompassed by the term polypeptide.

The term "antibody" is intended herein to encompass monoclonal antibody and polyclonal antibody.

The term "second messenger" shall mean an intracellular response produced as a result of receptor activation. A second messenger can include, for example, inositol 1,4,5-triphosphate (IP_3), diacylglycerol (DAG), cyclic AMP (cAMP), cyclic GMP (cGMP), MAP kinase acitivity, MAPK/ERK kinase kinase-1 (MEKK1) activity, and Ca^{2+}. Second messenger response can be measured for a determination of receptor activation.

The term "receptor functionality" shall refer to the normal operation of a receptor to receive a stimulus and moderate an effect in the cell, including, but not limited to regulating gene transcription, regulating the influx or efflux of ions, effecting a catalytic reaction, and/or modulating activity through G-proteins, such as eliciting a second messenger response.

The term "stimulate" or "stimulating," in relationship to the term "response" or "functionality of the receptor" shall mean that a response or a functionality of the receptor is increased in the presence of a compound as opposed to in the absence of the compound.

The term "inhibit" or "inhibiting," in relationship to the term "response" or "functionality of the receptor" shall mean that a response a functionality of the receptor is decreased or prevented in the presence of a compound as opposed to in the absence of the compound.

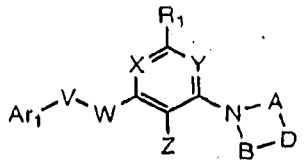
Where a range of values is provided, it is understood that each intervening value, to the tenth of the lower limit unless the context clearly indicates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the invention. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the invention, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the invention.

GPR119 Agonists

In certain embodiments, GPR119 is mammalian GPR119. In certain embodiments, GPR119 is rodent or primate GPR119. In certain embodiments, GPR119 is human GPR119.

The class of GPR119 agonists useful in compositions and methods of the present invention including but not limited to the novel therapeutic combinations of the present invention include compounds which exhibit an acceptably high affinity for GPR119 receptor. The GPR119 agonist or pharmaceutically acceptable salt may be any agonist, and in particular embodiment a selective GPR119 agonist.

Examples of GPR119 agonists are described in International Application No. PCT/US2004/001267 (published as WO 04/065380), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US2004/001267 as a GPR119 agonist is a compound of Formula (I):



(I) ;

wherein:

A and B are independently C_{1-3} alkylene optionally substituted with 1 to 4 methyl groups;

D is O, S, S(O), $S(O)_2$, CR_2R_3 or N-R_2;

V is selected from the group consisting of C_{1-3} alkylene, ethynylene and C_{1-2} heteroalkylene wherein each are optionally substituted with 1 to 4 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-4} alkoxy, carboxy, cyano, C_{1-3} haloalkyl and halogen; or

V is absent;

W is NR_4, O, S, S(O) or $S(O)_2$; or

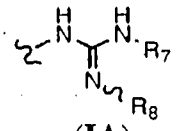
W is absent;

X is N or CR_5;

Y is N or CR_6;

Z is selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, C_{1-2} alkylamino, C_{2-4} dialkylamino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{4-8} diacylamino, C_{2-6} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} dialkylsulfonylamino, formyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylcarboxamide, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, halogen, aryl, heterocyclic, heteroaryl, hydroxyl, hydroxylamino, nitro and tetrazolyl, wherein C_{1-8} alkyl and C_{1-5} acyl are each optionally substituted with 1, 2, 3 or 4 groups selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-4} alkylcarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, C_{1-2} alkylamino, C_{2-4} dialkylamino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, formyl, C_{1-4} haloalkoxy, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, halogen, hydroxyl, hydroxylamino and nitro; or

Z is a group of Formula (IA):



(IA)

wherein:

R_7 is H, C_{1-8} alkyl or C_{3-6} cycloalkyl; and

R_8 is H, nitro or nitrile;

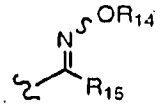
Ar_1 is aryl or heteroaryl wherein each are optionally substituted with R_9-R_{13};

R_1 is selected from the group consisting of H, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, C_{1-4} alkylamino, C_{2-8} dialkylamino, carboxamide, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio and hydroxyl;

R_2 is selected from the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-6} dialkylcarboxamide, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, heteroaryl, hydroxyl and phenyl; and wherein C_{1-8} alkyl, heteroaryl and phenyl are each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-3}-alkylene, C_{3-6}-cycloalkyl-C_{1-3}-heteroalkylene, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heterocyclic, hydroxyl, hydroxylamino and nitro; or

R_2 is -Ar_2-Ar_3 wherein Ar_2 and Ar_3 are independently aryl or heteroaryl each optionally substituted with 1 to 5 substituents selected from the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-6} dialkylcarboxamide, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, hydroxyl and nitro; or

R_2 is a group of Formula (**IB**):

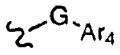


(IB)

wherein:

R_{14} is C_{1-8} alkyl or C_{3-6} cycloalkyl; and R_{15} is F, Cl, Br or CN; or

R_2 is a group of Formula (**IC**):



(IC)

wherein:

G is C=O, $CR_{16}R_{17}$, O, S, S(O), $S(O)_2$; where R_{16} and R_{17} are independently H or C_{1-8} alkyl; and

Ar_4 is phenyl or heteroaryl optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-6} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heteroaryl, hydroxyl, hydroxylamino and nitro;

R_3 is H, C_{1-8} alkyl, C_{1-4} alkoxy, halogen or hydroxyl;

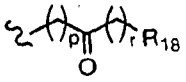
R_4 is H or C_{1-8} alkyl;

R_5 and R_6 are independently H, C_{1-8} alkyl or halogen;

R_9 is selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, arylsulfonyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heterocyclic, heterocyclicsulfonyl, heteroaryl, hydroxyl, nitro, C_{4-7} oxo-cycloalkyl, phenoxy, phenyl, sulfonamide and sulfonic acid, and wherein C_{1-5} acyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylsulfonamide, alkylsulfonyl, arylsulfonyl, heteroaryl, phenoxy and phenyl are each optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-}

$_{6}$cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heteroaryl, heterocyclic, hydroxyl, nitro and phenyl; or

R_9 is a group of Formula (**ID**):



(ID)

wherein:

"p" and "r" are independently 0, 1, 2 or 3; and

R_{18} is H, C_{1-5} acyl, C_{2-6} alkenyl, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, heteroaryl or phenyl, and wherein the heteroaryl and phenyl are each optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-4} alkoxy, amino, C_{1-4} alkylamino, C_{2-6} alkynyl, C_{2-8} dialkylamino, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl and hydroxyl; and

R_{10}-R_{13} are independently selected form the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl and nitro; or

two adjacent R_{10}-R_{11} groups together with Ar_1 form a 5, 6 or 7 membered cycloalkyl, cycloalkenyl or heterocyclic group wherein the 5, 6 or 7 membered group is optionally substituted with halogen.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/001267 include the following compounds according to Formula (**I**) (referred to herein as **Group A1**): [6-(4-Benzenesulfonyl-piperidin-1-yl)-5-nitro-pyrimidin-4-yl]-(4-methanesulfonyl-phenyl)-amine; {4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperazin-1-yl}-acetic acid ethyl ester; (2-Fluoro-phenyl)-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 1-[6-(4-Imidazol-1-yl-phenoxy)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[5-Nitro-6-(4-[1,2,4]triazol-1-yl-phenoxy)-pyrimidin-4-yl]-piperidine-4-

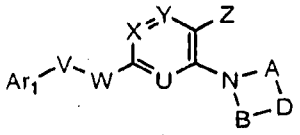
carboxylic acid ethyl ester; {6-[4-(4-Fluoro-phenoxy)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; {6-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; {6-[4-(3-Cyclopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; (4-Methanesulfonyl-phenyl)-(5-nitro-6-{4-[3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-piperidin-1-yl}-pyrimidin-4-yl)-amine; {6-[4-(3-Ethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(2-fluoro-phenyl)-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine; {6-[4-(3-Ethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(2-fluoro-4-methanesulfonyl-phenyl)-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[4-(3-propyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; {6-[4-(3-Cyclopropylmethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[4-(pyridin-4-yloxy)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[4-(pyrimidin-2-yloxy)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 1-[6-(4-Carbamoylmethyl-phenoxy)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-{6-[4-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-phenoxy]-5-nitro-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; 4'-[4-(2-Methoxycarbonyl-acetyl)-phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; {6-[4-(2-Methoxy-phenylsulfanyl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-[1,2,4]triazol-1-yl-phenyl)-amine; 4'-(2-Amino-4-ethanesulfonyl-phenoxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 4'-(4-Imidazol-1-yl-phenoxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; (4-Methoxy-2-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yloxy}-phenyl)-phenyl-methanone; 4-{4-[6-(4-Cyclopropylmethoxymethyl-piperidin-1-yl)-5-nitro-pyrimidin-4-yloxy]-phenyl}-butan-2-one; 4-{4-[5-Nitro-6-(4-propoxymethyl-piperidin-1-yl)-pyrimidin-4-yloxy]-phenyl}-butan-2-one; 4-{4-[6-(4-Butoxymethyl-piperidin-1-yl)-5-nitro-pyrimidin-4-yloxy]-phenyl}-butan-2-one; 4-{4-[6-(4-Isobutoxymethyl-piperidin-1-yl)-5-nitro-pyrimidin-4-yloxy]-phenyl}-butan-2-one; {1-[6-(Benzo[1,3]dioxol-5-ylamino)-5-nitro-pyrimidin-4-yl]-piperidin-4-yl}-(4-fluoro-phenyl)-methanone; (2,3-Difluoro-phenyl)-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (2,4-Difluoro-phenyl)-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 1-{2-Nitro-3-[4-(3-oxo-butyl)-phenoxy]-phenyl}-piperidine-4-carboxylic acid ethyl ester; 1-[6-(4-Acetyl-phenoxy)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 3'-Nitro-2'-[4-(3-oxo-butyl)-phenoxy]-3,4,5,6-tetrahydro-2H-[1,4']bipyridinyl-4-carboxylic acid ethyl ester; 4-(4-{5-Nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yloxy}-phenyl)-butan-2-one; 4-(4-{5-Nitro-6-[4-(2-trifluoromethyl-phenoxy)-piperidin-1-yl]-pyrimidin-4-yloxy}-phenyl)-butan-2-one; 4-(4-{6-[4-(3-Methyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yloxy}-phenyl)-butan-2-one; 4-(2,4-Difluoro-phenoxy)-5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidine; 4-(4-{6-[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yloxy}-phenyl)-butan-2-one; 4-(4-

Methanesulfonyl-phenoxy)-5-nitro-6-[4-(pyridin-2-ylsulfanyl)-cyclohexyl]-pyrimidine; 4-(4-Methanesulfonyl-phenoxy)-5-nitro-6-[4-(pyridin-4-ylsulfanyl)-cyclohexyl]-pyrimidine; 4-(4-Methanesulfonyl-phenoxy)-5-nitro-6-(4-phenylsulfanyl-cyclohexyl)-pyrimidine; 1-{6-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-5-nitro-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; 1-{6-[4-(1,1-Dioxo-1λ^6-thiomorpholin-4-ylmethyl)-phenylamino]-5-nitro-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; 1-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(4-Dimethylsulfamoyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(3-Methoxy-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(2-Methoxy-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(4-Methanesulfonyl-phenoxy)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester;1-{6-[4-(2-Methoxycarbonyl-acetyl)-phenoxy]-5-nitro-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; 1-[6-(2-Amino-4-ethanesulfonyl-phenoxy)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(2,5-Dimethoxy-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; (4-{5-Nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-ylamino}-phenyl)-phenyl-methanone; 1-[6-(4-Cyclohexyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[5-Nitro-6-(4-[1,2,4]triazol-1-yl-phenylamino)-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[5-Nitro-6-(4-trifluoromethanesulfonyl-phenylamino)-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[5-Nitro-6-(4-[1,2,3]thiadiazol-4-yl-phenylamino)-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; [6-(4-Ethoxymethyl-piperidin-1-yl)-5-nitro-pyrimidin-4-yl]-(4-methanesulfonyl-phenyl)-amine; [5-Nitro-6-(4-propyl-piperidin-1-yl)-pyrimidin-4-yl]-(4-[1,2,4]triazol-1-yl-phenyl)-amine; {5-Nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-(4-[1,2,4]triazol-1-yl-phenyl)-amine; (2-Fluoro-phenyl)-{6-[4-(3-methyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine; (4-Methanesulfonyl-phenyl)-{6-[4-(3-methyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine; {6-[4-(3-Methyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-[1,2,4]triazol-1-yl-phenyl)-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (3-Methoxy-phenyl)-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 1-[6-(Benzo[1,3]dioxol-5-ylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(2-Fluoro-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(3-Fluoro-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(3,4-Dihydro-2H-benzo[b][1,4]dioxepin-7-ylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-{6-[4-(Morpholine-4-sulfonyl)-phenylamino]-5-nitro-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; Benzo[1,3]dioxol-5-yl-[5-nitro-6-(4-propyl-piperidin-1-yl)-pyrimidin-4-yl]-amine; (4-Fluoro-phenyl)-{1-[5-nitro-6-(4-[1,2,4]triazol-1-yl-phenylamino)-pyrimidin-4-yl]-piperidin-4-yl}-methanone; [5-Nitro-6-(4-phenylsulfanyl-piperidin-1-yl)-pyrimidin-4-yl]-(4-[1,2,4]triazol-1-yl-phenyl)-amine; (4-Fluoro-phenyl)-{1-[6-(2-fluoro-phenylamino)-5-nitro-

pyrimidin-4-yl]-piperidin-4-yl}-methanone; (4-Methanesulfonyl-phenyl)-[5-nitro-6-(4-phenylsulfanyl-piperidin-1-yl)-pyrimidin-4-yl]-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[4-(pyridin-2-yloxy)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[4-(pyridin-4-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (4-Methanesulfonyl-phenyl)-{6-[4-(4-methoxy-phenylsulfanyl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine; 2-Methoxy-phenyl)-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (4-Methanesulfonyl-phenyl)-(5-nitro-6-{4-[3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-piperidin-1-yl}-pyrimidin-4-yl)-amine; {6-[4-(3-Ethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; (6-{4-[5-(4-Fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-piperidin-1-yl}-5-nitro-pyrimidin-4-yl)-(4-methanesulfonyl-phenyl)-amine; (4-Methanesulfonyl-phenyl)-[5-nitro-6-(4-pyridin-2-ylmethyl-piperidin-1-yl)-pyrimidin-4-yl]-amine; 1-{6-[4-(2,5-Dioxo-imidazolidin-4-yl)-phenoxy]-5-nitro-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; 1-[5-Nitro-6-(4-propionyl-phenoxy)-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[5-Nitro-6-(4-[1,2,3]thiadiazol-4-yl-phenoxy)-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-[4-(3-Oxo-butyl)-phenoxy]-5-(2,2,2-trifluoro-acetylamino)-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-[6-(2-Benzoyl-5-methoxy-phenoxy)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 3'-Nitro-4'-[4-(3-oxo-butyl)-phenoxy]-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 1-[6-(4-Dimethyl sulfamoyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidine-4-carboxylic acid ethyl ester; 1-{6-[4-(4,5-Dichloro-imidazol-1-yl)-phenylamino]-5-nitro-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; Benzo[1,3]dioxol-5-yl-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (4-Fluoro-phenyl)-{1-[6-(2-fluoro-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidin-4-yl}-methanone; (2,5-Difluoro-phenyl)-{5-nitro-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 1-{5-Nitro-6-[4-(3-oxo-butyl)-phenoxy]-pyrimidin-4-yl}-piperidine-4-carboxylic acid ethyl ester; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methanesulfonyl-phenoxy)-pyrimidine-5-carbonitrile; 5-[1,3]Dioxolan-2-yl-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methanesulfonyl-phenoxy)-pyrimidine; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methanesulfonyl-phenoxy)-pyrimidine-5-carbaldehyde; 5-[1,3]Dioxolan-2-yl-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-[1,2,3]thiadiazol-4-yl-phenoxy)-pyrimidine; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-[1,2,3]thiadiazol-4-yl-phenoxy)-pyrimidine-5-carbaldehyde; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-[1,2,3]thiadiazol-4-yl-phenoxy)-pyrimidine-5-carboxylic acid; [4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-[1,2,3]thiadiazol-4-yl-phenoxy)-pyrimidin-5-yl]-methanol; [4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-[1,2,3]thiadiazol-4-yl-phenoxy)-pyrimidin-5-ylmethyl]-dimethyl-amine; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methylsulfanyl-phenylamino)-pyrimidine-5-carbonitrile; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methanesulfinyl-phenylamino)-pyrimidine-5-carbonitrile; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[4-(4-trifluoromethoxy-phenoxy)-piperidin-1-yl]-pyrimidin-4-

yl}-amine; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methanesulfonyl-phenylamino)-pyrimidine-5-carbonitrile; 1-{1-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidin-4-yl}-hexan-1-one; 1-{1-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperidin-4-yl}-hexan-1-one; {6-[4-(3-tert-Butyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(2-fluoro-4-methanesulfonyl-phenyl)-amine; {6-[4-(3-tert-Butyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; [6-(4-Benzofuran-2-yl-piperidin-1-yl)-5-nitro-pyrimidin-4-yl]-(4-methanesulfonyl-phenyl)-amine and 5-Nitro-4-(5-phenyl-[1,3,4]oxadiazol-2-ylsulfanyl)-6-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-pyrimidine.

Examples of GPR119 agonists are described in International Application No. PCT/US2004/005555 (published as WO 04/076413), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US2004/005555 as a GPR119 agonist is a compound of Formula (**II**):



(**II**)

wherein:

A and B are independently C_{1-3} alkylene optionally substituted with 1 to 4 methyl groups;

U is N or CR_1;

D is O, S, S(O), $S(O)_2$, CR_2R_3 or NR_2;

V is selected from the group consisting of C_{1-3} alkylene, ethynylene and C_{1-2} heteroalkylene optionally substituted with 1 to 4 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-4} alkoxy, carboxy, cyano, C_{1-3} haloalkyl and halogen; or V is absent;

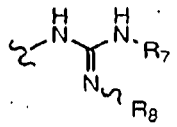
W is $-S(O)_2NR_4-$, $-NR_4-$, -O-, -S-, -S(O)-, $-S(O)_2-$; or W is absent;

X is N or CR_5;

Y is N or CR_6;

Z is selected from the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-6} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{4-8} diacylamino, C_{1-4} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} dialkylsulfonylamino, formyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylcarboxamide, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, halogen, aryl, heteroaryl, hydroxyl, hydroxylamino, nitro and tetrazolyl; or

Z is a group of Formula (**IIA**):



(IIA)

wherein:

R_7 is H, C_{1-6} alkyl or C_{3-6} cycloalkyl; and

R_8 is H, nitro or cyano;

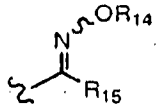
Ar_1 is aryl or heteroaryl optionally substituted with R_9, R_{10}, R_{11}, R_{12} and R_{13};

R_1, R_5 and R_6 are independently selected from the group consisting of H, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, C_{1-4} alkylamino, C_{2-8} dialkylamino, carboxamide, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl and nitro;

R_2 is selected from the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-6} dialkylcarboxamide, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, heteroaryl, hydroxyl and phenyl; and wherein C_{1-8} alkyl, heteroaryl and phenyl are optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-3}-heteroalkylene, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heterocyclic, hydroxyl, hydroxylamino and nitro; or

R_2 is -Ar_2-Ar_3 wherein Ar_2 and Ar_3 are independently aryl or heteroaryl optionally substituted with 1 to 5 substituents selected from the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-6} dialkylcarboxamide, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, hydroxyl and nitro; or

R_2 is a group of Formula (**IIB**):

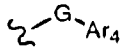


(IIB)

wherein:

R_{14} is C_{1-8} alkyl or C_{3-6} cycloalkyl; and R_{15} is F, Cl, Br or CN; or

R_2 is a group of Formula (IIC):



(IIC)

wherein:

G is C=O, $CR_{16}R_{17}$, O, S, S(O), $S(O)_2$; where R_{16} and R_{17} are independently H or C_{1-8} alkyl; and

Ar_4 is phenyl or heteroaryl optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-6} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heteroaryl, hydroxyl, hydroxylamino and nitro;

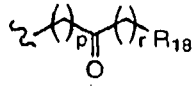
R_3 is H, C_{1-8} alkyl, C_{1-4} alkoxy or hydroxyl;

R_4 is H or C_{1-8} alkyl;

R_9 is selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, arylsulfonyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heterocyclic, heterocyclicsulfonyl, heteroaryl, hydroxyl, nitro, C_{4-7} oxo-cycloalkyl, phenoxy, phenyl, sulfonamide and sulfonic acid, and wherein C_{1-5} acyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylsulfonamide, alkylsulfonyl, arylsulfonyl, heteroaryl, phenoxy and phenyl are optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, C_{1-4}

haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heteroaryl, heterocyclic, hydroxyl, nitro and phenyl; or

R_9 is a group of Formula (**IID**):



(**IID**)

wherein:

"p" and "r" are independently 0, 1, 2 or 3; and

R_{18} is H, C_{1-5} acyl, C_{2-6} alkenyl, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, heteroaryl or phenyl, and wherein the heteroaryl or phenyl optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-4} alkoxy, C_{1-8} alkyl, amino, C_{1-4} alkylamino, C_{2-6} alkynyl, C_{2-8} dialkylamino, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl and hydroxyl; and

R_{10}-R_{13} are independently selected form the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl and nitro; or

two adjacent R_{10}-R_{11} groups form a 5, 6 or 7 membered cycloalkyl, cycloalkenyl or heterocyclic group with Ar_1 wherein the 5, 6 or 7 membered group is optionally substituted with halogen.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/005555 include the following compounds according to Formula (**II**) (referred to herein as **Group B1**): 6'-[4-(2-Methoxycarbonyl-acetyl)-phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 1-[4-(4-Acetyl-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-6'-yloxy)-phenyl]-ethanone; 6'-[4-(4-Hydroxy-benzenesulfonyl)-phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(4-Imidazol-1-yl-phenoxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(4-Benzoyl-phenoxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-[4-(2-Methoxy-ethyl)-

phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(4-Cyclopentyl-phenoxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(4'-Cyano-biphenyl-4-yloxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 3'-Nitro-6'-(4-sulfo-phenoxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 3'-Nitro-6'-(4-pyrrol-1-yl-phenoxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(4-Carbamoyl-phenoxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 3'-Nitro-6'-(4-[1,2,4]triazol-1-yl-phenoxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(2-Amino-4-ethanesulfonyl-phenoxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 3'-Nitro-6'-[4-(4-oxo-cyclohexyl)-phenoxy]-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(4'-Methoxy-biphenyl-4-yloxy)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 3'-Nitro-6'-(4-[1,2,3]thiadiazol-4-yl-phenoxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-[4-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-[4-(2,5-Dioxo-imidazolidin-4-yl)-phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 3'-Nitro-6'-[4-(3-oxo-butyl)-phenoxy]-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 3-[4-(3'-Nitro-4-propyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-6'-yloxy)-phenyl]-3-oxo-propionic acid methyl ester; 4-[4-(3'-Nitro-4-propyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-6'-yloxy)-phenyl]-butan-2-one; 4-{4-[3'-Nitro-4-(pyridin-2-ylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-6'-yloxy]-phenyl}-butan-2-one; and 3'-Nitro-4-(pyridin-2-ylsulfanyl)-6'-(4-[1,2,4]triazol-1-yl-phenoxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/005555 include the following compounds according to Formula (**II**) (referred to herein as **Group B2**): 1-[5-(4-Benzoyl-phenoxy)-2-nitro-phenyl]-piperidine-4-carboxylic acid ethyl ester; 1-{5-[4-(2-Methoxycarbonyl-acetyl)-phenoxy]-2-nitro-phenyl}-piperidine-4-carboxylic acid ethyl ester; 1-[5-(2-Amino-4-ethanesulfonyl-phenoxy)-2-nitro-phenyl]-piperidine-4-carboxylic acid ethyl ester; 1-{2-Nitro-5-[4-(3-oxo-butyl)-phenoxy]-phenyl}-piperidine-4-carboxylic acid ethyl ester; 4-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-butan-2-one; 1-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-ethanone; 3-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-3-oxo-propionic acid methyl ester; 5-Ethanesulfonyl-2-[4-nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenylamine; {4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-phenyl-methanone; 1-{4-Nitro-3-[4-(3-oxo-butyl)-phenoxy]-phenyl}-piperidine-4-carboxylic acid ethyl ester; 4-{4-[2-Nitro-5-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-butan-2-one; 1-[3-(4-Benzoyl-phenoxy)-4-nitro-phenyl]-piperidine-4-carboxylic acid ethyl ester; {4-[2-Nitro-5-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-phenyl-methanone; 1-{5-[4-(2-Carboxy-ethyl)-phenoxy]-2-nitro-phenyl}-piperidine-4-carboxylic acid ethyl ester; 1-{5-[4-(2-Carboxy-2-oxo-ethyl)-phenoxy]-2-nitro-phenyl}-piperidine-4-carboxylic acid ethyl ester; 1-[2-Nitro-5-(4-vinyl-phenoxy)-phenyl]-piperidine-4-

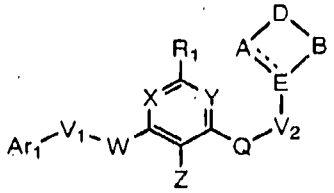
carboxylic acid ethyl ester; 3-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-propionic acid; 3-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-2-oxo-propionic acid; 1-[2-Nitro-5-(4-vinyl-phenoxy)-phenyl]-4-propyl-piperidine; 1-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-butan-1-one; 1-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-pentan-1-one; 1-{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-hexan-1-one; 4-{4-[3-(4-Methoxymethyl-piperidin-1-yl)-4-nitro-phenoxy]-phenyl}-butan-2-one; 1-{4-[3-(4-Methoxymethyl-piperidin-1-yl)-4-nitro-phenoxy]-phenyl}-ethanone; {4-[3-(4-Methoxymethyl-piperidin-1-yl)-4-nitro-phenoxy]-phenyl}-phenyl-methanone; 2-(3-Methyl-[1,2,4]oxadiazol-5-yl)-1-{4-[4-nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-ethanone; 4-(4-{3-[4-(3-Methyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-4-nitro-phenoxy}-phenyl)-butan-2-one; 4-(4-{4-Nitro-3-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-phenoxy}-phenyl)-butan-2-one; 2-{1-[2-Nitro-5-(4-[1,2,4]triazol-1-yl-phenoxy)-phenyl]-piperidin-4-ylsulfanyl}-pyridine; 2-Methyl-5-{4-[4-nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-phenyl}-2H-pyrazol-3-ol; 2-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-5-trifluoromethyl-pyridine; 5-Bromo-2-[4-nitro-3-(4-propyl-piperidin-1-yl)-phenoxy]-pyridine; 1-(4-{4-Nitro-3-[4-(pyridin-2-ylsulfanyl)-piperidin-1-yl]-phenoxy}-phenyl)-ethanone; 2-{1-[5-(4-Methanesulfonyl-phenoxy)-2-nitro-phenyl]-piperidin-4-ylsulfanyl}-pyridine; 1-{5-[4-(5-Methyl-[1,3,4]oxadiazol-2-yl)-phenoxy]-2-nitro-phenyl}-4-propyl-piperidine; 1-{5-[3-(3-Methyl-[1,2,4]oxadiazol-5-yl)-phenoxy]-2-nitro-phenyl}-4-propyl-piperidine.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/005555 include the following compound according to Formula (**II**) (referred to herein as **Group B3**): 5-Bromo-1-[4-nitro-3-(4-propyl-piperidin-1-yl)-phenyl]-1H-pyridin-2-one.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/005555 include the following compounds according to Formula (**II**) (referred to herein as **Group B4**): 6'-Benzenesulfonylamino-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(Benzenesulfonyl-methyl-amino)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(Benzenesulfonyl-butyl-amino)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(5-Ethanesulfonyl-2-hydroxy-phenylamino)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; 6'-(2-Bromo-4-trifluoromethyl-benzenesulfonylamino)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester; {4-[3'-Nitro-4-(pyridin-2-ylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-6'-ylamino]-phenyl}-phenyl-methanone and [3'-Nitro-4-(pyridin-2-ylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-6'-yl]-(4-[1,2,4]triazol-1-yl-phenyl)-amine.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/005555 include the following compounds according to Formula (**II**) (referred to herein as **Group B5**): 1-[5-(4-Benzoyl-phenylamino)-2-nitro-phenyl]-piperidine-4-carboxylic acid ethyl ester and {4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenylamino]-phenyl}-phenyl-methanone.

Examples of GPR119 agonists are described in International Application No. PCT/US2004/022327 (published as WO 05/007647), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US2004/022327 as a GPR119 agonist is a compound of Formula (**III**):



(III)

wherein:

A and B are each independently C_{1-3} alkylene optionally substituted with 1 to 4 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-4} alkoxy, carboxy, cyano, C_{1-3} haloalkyl and halogen;

D is O, S, S(O), $S(O)_2$, CR_2R_3 or N-R_2;

E is N, C or CR_4;

---- is a single bond when E is N or CR_4, or a double bond when E is C;

V_1 is selected from the group consisting of C_{1-3} alkylene, ethynylene and C_{1-2} heteroalkylene optionally substituted with 1 to 4 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-4} alkoxy, carboxy, cyano, C_{1-3} haloalkyl and halogen; or V_1 is a bond;

V_2 is C_{3-6} cycloalkylene or C_{1-3} alkylene wherein each are optionally substituted with 1 to 4 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-4} alkoxy, carboxy, cyano, C_{1-3} haloalkyl and halogen; or V_2 is a bond;

W is NR_5, O, S, S(O) or $S(O)_2$; or W is absent;

Q is NR_6, O, S, S(O) or $S(O)_2$;

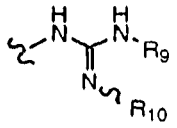
X is N or CR_7;

Y is N or CR_8;

Z is selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, C_{1-2} alkylamino, C_{2-4} dialkylamino, carbamimidoyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{4-8} diacylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{2-6} dialkylsulfonylamino, formyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylcarboxamide, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, halogen, aryl, heterocyclic, heteroaryl, hydroxyl, hydroxycarbamimidoyl, hydroxylamino, nitro and tetrazolyl, wherein C_{1-8} alkyl, C_{3-7} cycloalkyl, and heterocyclic are each optionally substituted with 1, 2, 3 or 4 groups selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-7} alkyl, C_{1-4} alkylcarboxamide, C_{1-4}

alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, C_{1-2} alkylamino, C_{2-4} dialkylamino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, formyl, C_{1-4} haloalkoxy, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, halogen, hydroxyl, hydroxylamino and nitro, and wherein said C_{1-7} alkyl is optionally substituted with amino; or

Z is a group of Formula (**IIIA**):



(**IIIA**)

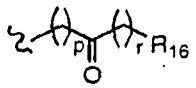
wherein:

R_9 is H, C_{1-8} alkyl or C_{3-7} cycloalkyl; and

R_{10} is H, nitro or nitrile;

Ar_1 is aryl or heteroaryl each optionally substituted with R_{11}, R_{12}, R_{13}, R_{14}, and R_{15}; wherein R_{11} is selected from the group consisting of C_{1-5} acyl, C_{1-6} acylsulfonamide, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-6} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, arylsulfonyl, carbamimidoyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{3-7} cycloalkyloxy, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, guanidinyl, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heterocyclic, heterocyclic-oxy, heterocyclicsulfonyl, heterocyclic-carbonyl, heteroaryl, heteroarylcarbonyl, hydroxyl, nitro, C_{4-7} oxo-cycloalkyl, phenoxy, phenyl, sulfonamide, sulfonic acid, and thiol, and wherein C_{1-5} acyl, C_{1-6} acylsulfonamide, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-6} alkylsulfonamide, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, arylsulfonyl, carbamimidoyl, C_{2-6} dialkylamino, heterocyclic, heterocyclic-carbonyl, heteroaryl, phenoxy and phenyl are optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-7} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{3-7} cycloalkyloxy, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heteroaryl, heterocyclic, hydroxyl, nitro, phenyl, and phosphonooxy, wherein said C_{1-7} alkyl and C_{1-4} alkylcarboxamide are each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-4} alkoxy and hydroxy; or

R_{11} is a group of Formula (**IIIB**):



(IIIB)

wherein:

"p" and "r" are each independently 0, 1, 2 or 3; and R_{16} is H, C_{1-5} acyl, C_{2-6} alkenyl, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, heteroaryl or phenyl, and wherein the heteroaryl or phenyl optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-4} alkoxy, amino, C_{1-4} alkylamino, C_{2-6} alkynyl, C_{2-8} dialkylamino, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl and hydroxyl; and

R_{12}, R_{13}, R_{14}, and R_{15} are each independently selected form the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl and nitro; or

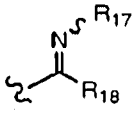
two adjacent groups selected from the group consisting of R_{12}, R_{13}, R_{14} and R_{15} together with the atoms to which they are attached form a 5-, 6- or 7-membered cycloalkyl, cycloalkenyl or heterocyclic group fused with Ar_1, wherein the 5-, 6- or 7-membered group is optionally substituted with halogen;

R_1, R_7 and R_8 are each independently selected from the group consisting of H, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, C_{1-4} alkylamino, C_{2-8} dialkylamino, carboxamide, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio and hydroxyl;

R_2 is selected from the group consisting of C_{1-8} alkyl, amino, aryl, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, heteroaryl and hydroxyl; and wherein C_{1-8} alkyl, aryl or heteroaryl optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-3}-heteroalkylene, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heterocyclic, hydroxyl, hydroxylamino and nitro; or

R_2 is -Ar_2-Ar_3 wherein Ar_2 and Ar_3 are each independently aryl or heteroaryl optionally substituted with 1 to 5 substituents selected from the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, amino, C_{1-4} alkylamino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, hydroxyl and nitro; or

R_2 is a group of Formula (**IIIC**):

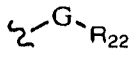


(IIIC)

wherein:

R_{17} is H, C_{1-8} alkyl, C_{3-7} cycloalkyl, aryl, heteroaryl or OR_{19}; and R_{18} is F, Cl, Br, CN or $NR_{20}R_{21}$; where R_{19} is H, C_{1-8} alkyl or C_{3-7} cycloalkyl, and R_{20} and R_{21} are each independently H, C_{1-8} alkyl, C_{3-7} cycloalkyl, aryl or heteroaryl; or

R_2 is a group of Formula (**IIID**):



(IIID)

wherein:

G is:

i) -C(O)-, -C(O)NR_{23}-, -C(O)O-, -OC(O)NR_{23}-, -NR_{23}C(O)O-, -OC(O) -, -C(S)-, -C(S)NR_{23}-, -C(S)O-, -OC(S)-, -$CR_{23}R_{24}$-, -O-, -S-, -S(O)- or -$S(O)_2$- when D is CR_2R_3, or

ii) -$CR_{23}R_{24}$C(O)-, -C(O)-, -$CR_{23}R_{24}$C(O)NR_{25}-, -C(O)NR_{23}-, -C(O)O-, -C(S)-, -C(S)NR_{23}-, -C(S)O-, -$CR_{23}R_{24}$-, -$S(O)_2$-, or a bond when D is NR_2,

wherein R_{23}, R_{24} and R_{25} are each independently H or C_{1-8} alkyl; and R_{22} is H, C_{1-8} alkyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, phenyl, heteroaryl, or heterocyclic each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-7} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heteroaryl, heterocyclic, hydroxyl, hydroxylamino, nitro, phenyl, phenoxy, and sulfonic acid, wherein said C_{1-7} alkyl, heteroaryl, phenyl and phenoxy are each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4}

alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heterocyclic, hydroxyl, hydroxylamino, and nitro;

R_3 is H, C_{1-8} alkyl, C_{1-4} alkoxy or hydroxyl; and

R_4, R_5 and R_6 are each independently H, C_{1-8} alkyl or C_{3-7} cycloalkyl, wherein said C_{1-8} alkyl is optionally substituted with C_{1-4} alkoxy, C_{3-7} cycloalkyl, or heteroaryl.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C1**): 3-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxymethyl]-pyrrolidine-1-carboxylic acid tert-butyl ester; 4-[5-Cyano-6-(6-methylsulfanyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[5-Cyano-6-(6-methanesulfonyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; [6-(1-Hexyl-piperidin-4-yloxy)-5-nitro-pyrimidin-4-yl]-(4-methanesulfonyl-phenyl)-amine; [6-(1-Cyclopropylmethyl-piperidin-4-yloxy)-5-nitro-pyrimidin-4-yl]-(4-methanesulfonyl-phenyl)-amine; 4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester; {4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidin-1-yl}-pyridin-3-yl-methanone; (2-Chloro-pyridin-3-yl)-{4-[6-(4-methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidin-1-yl}-pyridin-2-yl-methanone; (4-Methanesulfonyl-phenyl)-[6-(1-methanesulfonyl-piperidin-4-yloxy)-5-nitro-pyrimidin-4-yl]-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[1-(propane-1-sulfonyl)-piperidin-4-yloxy]-pyrimidin-4-yl}-amine; {6-[1-(Butane-1-sulfonyl)-piperidin-4-yloxy]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; (4-Methanesulfonyl-phenyl)-{5-nitro-6-[1-(thiophene-2-sulfonyl)-piperidin-4-yloxy]-pyrimidin-4-yl}-amine; (4-Methanesulfonyl-phenyl)-{6-[1-(1-methyl-1H-imidazole-4-sulfonyl)-piperidin-4-yloxy]-5-nitro-pyrimidin-4-yl}-amine; {6-[1-(2,4-Dimethyl-thiazole-5-sulfonyl)-piperidin-4-yloxy]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; 4-[5-Cyano-6-(3-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-

piperidine-1-carboxylic acid tert-butyl ester; 4-[5-Cyano-6-(4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Methanesulfonyl-pyridin-3-ylamino)-5-nitro-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[5-Acetyl-6-(6-methanesulfonyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[5-Amino-6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[5-Cyano-6-(4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid ethyl ester; 4-[5-Cyano-6-(4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isobutyl ester; 4-(4-Methanesulfonyl-phenylamino)-6-[1-(tetrahydro-furan-2-carbonyl)-piperidin-4-yloxy]-pyrimidine-5-carbonitrile; 4-[1-(3,3-Dimethyl-2-oxo-butyl)-piperidin-4-yloxy]-6-(4-methanesulfonyl-phenylamino)-pyrimidine-5-carbonitrile; 4-(4-Methanesulfonyl-phenylamino)-6-[1-(pyridine-3-carbonyl)-piperidin-4-yloxy]-pyrimidine-5-carbonitrile; 4-(1-Formyl-piperidin-4-yloxy)-6-(4-methanesulfonyl-phenylamino)-pyrimidine-5-carbonitrile and 4-(4-Methanesulfonyl-phenylamino)-6-[1-(pyridine-2-carbonyl)-piperidin-4-yloxy]-pyrimidine-5-carbonitrile.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C2**): 4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; (4-Methanesulfonyl-phenyl)-[5-nitro-6-(piperidin-4-yloxy)-pyrimidin-4-yl]-amine; 1-{4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidin-1-yl}-3,3-dimethyl-butan-1-one; (4-Methanesulfonyl-phenyl)-[5-nitro-6-(1-pyridin-2-ylmethyl-piperidin-4-yloxy)-pyrimidin-4-yl]-amine; (4-Methanesulfonyl-phenyl)-[5-nitro-6-(1-pyridin-3-ylmethyl-piperidin-4-yloxy)-pyrimidin-4-yl]-amine; {6-[1-(3,3-Dimethyl-butyl)-piperidin-4-yloxy]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; (4-Methanesulfonyl-phenyl)-{6-[1-(3-methyl-butyl)-piperidin-4-yloxy]-5-nitro-pyrimidin-4-yl}-amine; (4-Methanesulfonyl-phenyl)-[5-nitro-6-(3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-yloxy)-pyrimidin-4-yl]-amine; 4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid ethyl ester; 1-{4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidin-1-yl}-3,3-dimethyl-butan-2-one; {6-[1-(2-Ethoxy-ethyl)-piperidin-4-yloxy]-5-nitro-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; 4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxymethyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-{2-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-ethyl}-piperidine-1-carboxylic acid tert-butyl ester; 3-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-pyrrolidine-1-carboxylic acid tert-butyl ester and 3-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxymethyl]-pyrrolidine-1-carboxylic acid tert-butyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C3**): 4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-ylamino]-piperidine-1-

carboxylic acid tert-butyl ester; N-(4-Methanesulfonyl-phenyl)-5-nitro-N'-piperidin-4-yl-pyrimidine-4,6-diamine; 1-{4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-ylamino]-piperidin-1-yl}-ethanone and 1-{4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-ylamino]-piperidin-1-yl}-2,2-dimethyl-propan-1-one.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C4**): 4-[6-(4-Cyano-2-fluoro-phenylamino)-5-ethynyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Ethynyl-6-(2-fluoro-4-[1,2,4]triazol-1-yl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Ethynyl-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrimidin-4-ylamino}-3-fluoro-benzonitrile; {5-Ethynyl-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrimidin-4-yl}-(2-fluoro-4-methanesulfonyl-phenyl)-amine; 4-{6-[2,5-Difluoro-4-(2-methanesulfonyl-ethyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-sulfamoyl-ethyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Fluoro-ethyl)-2-methyl-pyridin-3-ylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[4-Fluoro-6-(2-isopropoxy-ethyl)-pyridin-3-ylamino]-3-methyl-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-[1,2,4]triazol-1-yl-ethyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Ethynyl-6-[2-fluoro-4-(4-methoxy-pyridin-2-yl)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-propionylsulfamoyl-ethyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-methanesulfonyl-ethyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; and 4-{6-[2,3-Difluoro-4-(2-methanesulfonyl-ethyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C5**): 4-[5-Acetyl-6-(6-methanesulfonyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isobutyl ester; 1-[4-(1-Benzyl-azetidin-3-yloxy)-6-(6-methanesulfonyl-pyridin-3-ylamino)-pyrimidin-5-yl]-ethanone; 4-[5-Cyano-6-(6-propylamino-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(2-fluoro-4-isopropylamino-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(2-fluoro-4-propylamino-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(2-fluoro-4-propoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(6-propyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Cyano-6-[4-(2-dimethylamino-ethylsulfanyl)-2-fluoro-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Cyano-6-[4-(2-dimethylamino-ethanesulfonyl)-2-fluoro-phenylamino]-3-oxy-pyrimidin-4-yloxy}-piperidine-1-

carboxylic acid isopropyl ester; 4-{5-Cyano-6-[2-fluoro-4-(4-methyl-piperazin-1-yl)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Cyano-6-[2-fluoro-4-(3-methyl-butylamino)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(2-fluoro-4-morpholin-4-yl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Cyano-6-[4-(2-dimethylamino-ethylamino)-2-fluoro-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(4-dimethylamino-2-fluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Cyano-6-[2-fluoro-4-(2-pyrrolidin-1-yl-ethylamino)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Cyano-6-[2-fluoro-4-(2-morpholin-4-yl-ethylamino)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-iodo-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyano-6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-morpholin-4-yl-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-propoxy-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-propylamino-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-methoxy-ethylamino)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[(tetrahydro-furan-2-ylmethyl)-amino]-phenylamino}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-methanesulfonyl-ethylamino)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[(2-methanesulfonyl-ethyl)-methyl-amino]-phenylamino}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Bromo-2,5-difluoro-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Cyano-2-fluoro-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Cyano-2,5-difluoro-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-morpholin-4-yl-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Chloro-2-methyl-pyridin-3-ylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Methyl-6-(2-methyl-6-morpholin-4-yl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-(4,5-Dihydro-1H-imidazol-2-yl)-6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-5-methyl-pyrimidin-4-yl}-amine; 4-[6-(2-Fluoro-4-propoxy-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-methanesulfonyl-ethoxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-methoxy-ethoxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic

acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-isopropoxy-ethoxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Chloro-4-methyl-pyridin-3-ylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-(N-hydroxycarbamimidoyl)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Carbamimidoyl-6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(tetrahydro-furan-2-ylmethoxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Methyl-6-(4-methyl-6-morpholin-4-yl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methoxy-ethoxy)-2-methyl-pyridin-3-ylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methoxy-ethoxy)-4-methyl-pyridin-3-ylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-methoxy-ethoxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-isopropoxy-ethylsulfamoyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(N-hydroxycarbamimidoyl)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Carbamoyl-2,5-difluoro-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[(2-Fluoro-4-methanesulfonyl-phenyl)-(2-methoxy-ethyl)-amino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Carbamimidoyl-2,5-difluoro-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-(2-Ethoxy-ethoxy)-2-fluoro-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(tetrahydro-pyran-4-yloxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-hydroxy-ethoxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-butan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-pentan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methyl-butan-1-one; 4-{6-[2-Fluoro-4-(pyridin-2-ylmethoxy)-phenylamino]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2-Fluoro-4-methanesulfonyl-phenylamino)-3-methyl-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Chloro-4-fluoro-pyridin-3-ylamino)-5-cyano-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; and 4-[5-Amino-6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compound according to Formula (**III**) (referred to herein as **Group C6**): 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-yl]-isopropyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C7**): 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-6-[1-(3-methoxy-propyl)-piperidin-4-yloxy]-5-methyl-pyrimidine; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methoxy-propan-2-ol; 4-{6-[2-Fluoro-4-(5-isopropoxymethyl-[1,2,4]oxadiazol-3-yl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(5-methoxy-pyridin-2-yl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Cyclopropoxy-ethylamino)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(pyridine-2-carbonyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methanesulfonylamino-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Methoxy-6'-methyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yloxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-2-(4-trifluoromethoxy-phenoxy)-propan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-2-(4-trifluoromethoxy-phenoxy)-ethanone; N-(4-Chloro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-acetamide; N-(3-Chloro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-acetamide; N-(3,5-Dichloro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-acetamide; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-N-(4-trifluoromethyl-phenyl)-acetamide; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-N-phenyl-acetamide; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-N-(4-isopropyl-phenyl)-acetamide; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-N-(4-methoxy-phenyl)-acetamide; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-N-(3-trifluoromethyl-phenyl)-acetamide; 4-{6-[2-Fluoro-4-(3-methoxy-propane-1-sulfonyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Isopropoxy-ethyl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Methyl-6-[2-methyl-6-(2-pyridin-2-yl-ethoxy)-pyridin-3-yloxy]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(thiophene-2-carbonyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{6-[(2-Isopropoxy-ethyl)-methyl-amino]-2-methyl-pyridin-3-yloxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Isopropoxy-ethanesulfonyl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Hydroxy-ethanesulfonyl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Amino-2-methyl-pyridin-3-yloxy)-5-methyl-pyrimidin-4-

yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-6-[1-(3-methyl-butyl)-piperidin-4-yloxy]-pyrimidine; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-morpholin-4-yl-ethanone; 1-(3,4-Dichloro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(3-Chloro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-thiophen-3-yl-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-phenyl-ethanone; 1-(2,4-Dimethoxy-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-6-[1-(4-methyl-pentyl)-piperidin-4-yloxy]-pyrimidine; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-isopropoxy-propan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-4-isopropoxy-butan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-hydroxy-propan-1-one; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(5-pyridin-2-yl-thiophen-2-yl)-ethanone; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-6-[1-(5-methyl-hexyl)-piperidin-4-yloxy]-pyrimidine; 3-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-oxo-propane-1-sulfonic acid; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-thiophen-2-yl-ethanone; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-6-(1-pentyl-piperidin-4-yloxy)-pyrimidine; 4-(1-Butyl-piperidin-4-yloxy)-6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidine; 4-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-cyclohexanecarboxylic acid; 1-(4-Diethylamino-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(2-methyl-4-phenyl-furan-3-yl)-ethanone; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-6-(1-hexyl-piperidin-4-yloxy)-5-methyl-pyrimidine; 4-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-butyric acid; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-pentan-2-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-hexan-2-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-hexan-2-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-4-methyl-pentan-2-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-5-methyl-hexan-2-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-6-methyl-heptan-2-one; 5-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-4-oxo-pentanoic acid; 5-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-4-oxo-pentanenitrile; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-

phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-2-pyridin-2-yl-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-pyridin-4-yl-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-ylmethyl}-acrylic acid; 1-[1,4]Dioxan-2-yl-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(2,3-Dihydro-[1,4]dioxin-2-yl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-p-tolyl-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(4-methoxy-phenyl)-ethanone; 1-(2-Chloro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 3-(2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-acetyl)-benzonitrile; 1-(2,4-Dimethyl-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(4-Chloro-3-methyl-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(4-Difluoromethoxy-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(5-phenyl-thiophen-2-yl)-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-thiophen-2-yl-ethanone; {4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-acetic acid ethyl ester; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methoxy-propan-2-ol; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-6-[1-(4-methoxy-cyclohexyl)-piperidin-4-yloxy]-5-methyl-pyrimidine; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-hexan-1-one; 4-{6-[2-Fluoro-4-(2-isobutoxy-ethoxy)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-(2-Cyclopropoxy-ethoxy)-2-fluoro-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-(2-Ethoxy-ethoxy)-2-fluoro-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(3-methoxy-propoxy)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-pyridin-2-yl-ethoxy)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(tetrahydro-pyran-4-yloxy)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-(2-tert-Butoxy-ethoxy)-2-fluoro-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-sulfo-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-trifluoromethoxy-phenoxy)-5-ethynyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-trifluoromethoxy-phenoxy)-5-prop-1-ynyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Ethynyl-6-(2-fluoro-4-methoxy-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid

isopropyl ester; 4-[5-Ethynyl-6-(6-methoxy-4-methyl-pyridin-3-yloxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Ethynyl-6-[6-(2-isopropoxy-ethyl)-2-methyl-pyridin-3-yloxy]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Cyano-2-fluoro-phenoxy)-5-ethynyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Ethynyl-6-(2-fluoro-4-[1,2,4]triazol-4-yl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Ethynyl-6-(2-fluoro-4-[1,2,4]triazol-1-yl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 1-{4-[5-Ethynyl-6-(2-fluoro-4-[1,2,4]triazol-1-yl-phenoxy)-pyrimidin-4-yloxy]-piperidin-1-yl}-3-pyridin-2-yl-propan-1-one; 4-{5-Ethynyl-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrimidin-4-yloxy}-3-fluoro-benzonitrile; 5-Ethynyl-4-(2-fluoro-4-methanesulfonyl-phenoxy)-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrimidine; 4-[1-(3-Ethyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-5-ethynyl-6-(2-fluoro-4-methanesulfonyl-phenoxy)-pyrimidine; 4-[1-(3-Ethyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidine; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-6-[1-(3-methyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrimidine; 4-[6-(2-Fluoro-4-methanesulfonylamino-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; *cis*-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-cyclohexyl}-carbamic acid isopropyl ester; *trans*-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-cyclohexyl}-carbamic acid isopropyl ester; N-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-cyclohexyl}-3-methyl-butyramide; N-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-cyclohexyl}-isobutyramide; 4-{6-[2,5-Difluoro-4-(2-methanesulfonyl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-Fluoro-6-(2-methanesulfonyl-ethyl)-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Cyclopropyl-6-[2,5-difluoro-4-(2-hydroxy-ethyl)-phenoxy]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(5-Cyclopropyl-6-{2,5-difluoro-4-[2-(4-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-morpholin-4-yl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[2-(4-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Fluoro-ethyl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(1-hydroxy-cyclopropylmethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2,5-Difluoro-4-(2-methanesulfonyl-ethyl)-phenoxy]-3-methyl-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; (R)-4-(6-{2-Fluoro-4-[2-(3-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; (S)-4-(6-{2-Fluoro-4-[2-(3-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; (R)-4-(5-Ethynyl-6-{2-fluoro-4-[2-(2-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; (S)-4-(2-{2-Fluoro-

4-[2-(2-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-3-methyl-pyridin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-Fluoro-6-(2-morpholin-4-yl-ethyl)-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Ethynyl-6-[4-fluoro-6-(2-methanesulfonyl-ethyl)-pyridin-3-yloxy]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2,5-Difluoro-4-(2-isopropoxy-ethyl)-phenoxy]-3-methyl-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-propionylsulfamoyl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-sulfamoyl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-sulfamoyl-ethyl)-phenoxy]-5-ethynyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-[1,2,4]triazol-1-yl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,3-Difluoro-4-(2-methanesulfonyl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(2-{2-Fluoro-4-[2-(6-methoxy-pyridin-2-yl)-ethyl]-phenoxy}-3-methyl-pyridin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[2-(3-methoxy-pyridin-2-yl)-ethyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3-Fluoro-1-oxy-pyridin-4-yloxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5'-Methoxy-6-methyl-[2,2']bipyridinyl-5-yloxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Ethynyl-6-[2-fluoro-4-(4-methoxy-pyridin-2-yl)-phenoxy]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(3-methoxy-pyridin-2-yl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2,5-Difluoro-4-[2-(3-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; and 4-(6-{2,5-Difluoro-4-[2-(3-methoxy-piperidin-1-yl)-ethyl]-phenoxy}-5-ethynyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C8**): 4-[6-(2-Fluoro-4-morpholin-4-yl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; {4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-[6-(2-pyrrolidin-1-yl-ethyl)-pyridin-3-yl]-methanone; (6-Amino-pyridin-3-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 4-[5-Ethyl-6-(2-fluoro-4-methanesulfonyl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Isopropoxy-ethylamino)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Hydroxy-ethylsulfanyl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Methyl-6-(2-methyl-6-pentyl-pyridin-3-yloxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(3-fluoro-phenyl)-ethanone; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-

methyl-6-[1-(2-pyridin-3-yl-ethyl)-piperidin-4-yloxy]-pyrimidine; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(4-trifluoromethoxy-phenyl)-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-pyridin-2-yl-ethanone; 4-{6-[6-(2-Methoxy-ethanesulfonyl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(2-Fluoro-4-methanesulfonyl-phenoxy)-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-5-methyl-pyrimidine; 4-(6-{2-Fluoro-4-[(2-hydroxy-ethylcarbamoyl)-methyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Iodo-pyridin-2-yloxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[N-(2-isopropoxy-ethyl)-carbamimidoyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Carboxy-2-fluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-(4-Bromo-2-fluoro-phenoxy)-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-5-methyl-pyrimidine; 4-[6-(5-Methanesulfonyl-pyridin-2-yloxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Hydroxy-ethylamino)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Cyclopropyl-6-(2-fluoro-4-methanesulfonyl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methanesulfonyl-ethylamino)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-4-oxo-butyric acid; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(3-trifluoromethyl-phenyl)-ethanone; 4-{6-[6-(2-Methoxy-ethylsulfanyl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 1-(2,5-Dimethoxy-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-pyridin-2-yl-ethanone; 4-[6-(6-Chloro-2-methyl-pyridin-3-yloxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(4-fluoro-phenyl)-ethanone; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(4-trifluoromethyl-phenyl)-ethanone; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3,3-dimethyl-butan-2-one; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-pyridin-3-yl-ethanone; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-butan-2-one; 4-(6-{2-Fluoro-4-[(2-isopropoxy-ethylcarbamoyl)-methyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-(4-methanesulfonyl-phenyl)-ethanone; 1-(4-Chloro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 4-(2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-acetyl)-

benzonitrile; 1-(3,4-Difluoro-phenyl)-2-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 4-{6-[2-Fluoro-4-(2-isopropoxy-ethylcarbamoyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-butan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-pentan-1-one; 4-[6-(2,4-Difluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methyl-butan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-4-methyl-pentan-1-one; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-5-methyl-hexan-1-one; 4-{6-[2-Fluoro-4-(2-methoxy-ethylcarbamoyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Bromo-2-fluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(methoxy-methyl-carbamoyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methoxy-propan-1-one; 4-[6-(4-Cyano-2-fluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-(5-Aminomethyl-4,5-dihydro-oxazol-2-yl)-6-(2-fluoro-4-methanesulfonyl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methoxy-ethylamino)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(3-Methanesulfonyl-pyrrolidin-1-yl)-2-methyl-pyridin-3-yloxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Benzylamino-2-methyl-pyridin-3-yloxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Carbamoyl-2-fluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-isopropoxy-ethylamino)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[(tetrahydro-furan-2-ylmethyl)-amino]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{6-[(2-Methanesulfonyl-ethyl)-methyl-amino]-2-methyl-pyridin-3-yloxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-hydroxycarbamoyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-pyrrolidin-1-yl-ethylcarbamoyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(4-isopropyl-piperazine-1-carbonyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-morpholin-4-yl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-methanesulfonyl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-hydroxy-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Carboxymethyl-2-fluoro-phenoxy)-5-methyl-

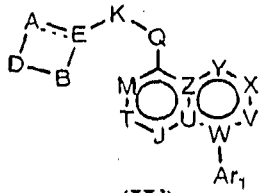
pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Dimethylcarbamoylmethyl-2-fluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-sulfamoyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-propionylsulfamoyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Ethynyl-6-(2-fluoro-4-methanesulfonyl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-phosphonooxy-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Bromo-6-(2-fluoro-4-methanesulfonyl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[2-(2-methanesulfonyl-pyrrolidin-1-yl)-2-oxo-ethyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Carbamoylmethyl-2-fluoro-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-{[(tetrahydro-furan-2-ylmethyl)-carbamoyl]-methyl}-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-3-sulfamoyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; C-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-C-(4-fluoro-phenyl)-methyleneamine; 3-tert-Butoxy-1-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-propan-1-one; 2-Ethoxy-1-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; {4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-(tetrahydro-furan-2-yl)-methanone; (S)-1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methyl-2-methylamino-butan-1-one; 4-(6-{2-Fluoro-4-[2-(3-hydroxy-piperidin-1-yl)-2-oxo-ethyl]-phenoxy}-5-methyl-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-morpholin-4-yl-2-oxo-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-imidazol-1-yl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-[1,2,3]triazol-1-yl-ethyl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; (R)-1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methyl-2-methylamino-butan-1-one; (S)-1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-hydroxy-butan-1-one; (R)-N-(1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carbonyl}-2-methyl-propyl)-acetamide; (S)-N-(1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carbonyl}-2-methyl-propyl)-acetamide; (R)-N-(2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-methyl-2-oxo-ethyl)-acetamide; (S)-N-(2-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-1-methyl-2-oxo-ethyl)-acetamide; 4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid (S)-tetrahydro-furan-3-yl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid (R)-tetrahydro-furan-3-yl ester; 4-[6-(2-

Amino-4-ethanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; (1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carbonyl}-2-methyl-propyl)-carbamic acid tert-butyl ester; 4-{6-[2-Fluoro-4-(6-methoxy-pyridin-3-yl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 3-Amino-1-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-4-methyl-pentan-1-one; 2-Amino-1-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methyl-butan-1-one; 4-{6-[2-Fluoro-4-(2-isopropoxy-ethoxy)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; and 4-[5-Methyl-6-(4-sulfo-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compounds according to Formula (**III**) (referred to herein as **Group C9**): 4-({Cyclopropyl-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Cyclopropyl-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yl]-isopropyl-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; and 4-({Cyclopropylmethyl-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022327 include the following compound according to Formula (**III**) (referred to herein as **Group C10**): 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid isopropyl ester.

Examples of GPR119 agonists are described in International Application No. PCT/US2004/022417 (published as WO 05/007658), the disclosure of each of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US2004/022417 as a GPR119 agonist is a compound of Formula (**IV**):



(**IV**) ;

wherein:

A and B are each independently C_{1-3} alkylene optionally substituted with 1 to 4 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-4} alkoxy, carboxy, cyano, C_{1-3} haloalkyl and halogen;

D is O, S, S(O), $S(O)_2$, CR_1R_2 or N-R_2, wherein R_1 is selected from the group consisting of H, C_{1-8} alkyl, C_{1-4} alkoxy, halogen and hydroxyl;

E is N, C or CR_3, wherein R_3 is H or C_{1-8} alkyl;

---- is a single bond when E is N or CR_3, or a double bond when E is C;

K is a C_{3-6} cycloalkylene or C_{1-3} alkylene wherein each are optionally substituted with 1 to 4 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-4} alkoxy, carboxy, cyano, C_{1-3} haloalkyl and halogen; or K is a bond;

Q is NR_4, O, S, S(O) or $S(O)_2$, wherein R_4 is H or C_{1-8} alkyl and the C_{1-8} alkyl is optionally substituted with C_{2-8} dialkylamine;

T is N or CR_5;

M is N or CR_6;

J is N or CR_7;

U is C or N;

V is N, CR_8 or V is a bond;

W is N or C;

X is O, S, N, CR_9 or NR_{11};

Y is O, S, N, CR_{10} or NR_{12};

Z is C or N;

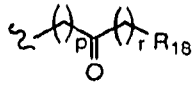
R_5, R_6, R_7, R_8, R_9 and R_{10} are each independently selected from the group consisting of H, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, C_{1-4} alkylamino, C_{2-8} dialkylamino, carboxamide, cyano, C_{3-6} cycloalkyl, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylsulfonamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl, hydroxylamino and nitro; wherein said C_{2-6} alkenyl, C_{1-8} alkyl, C_{2-6} alkynyl and C_{3-6} cycloalkyl are optionally substituted with 1, 2, 3 or 4 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, hydroxyl, hydroxylamino and nitro;

R_{11} and R_{12} are each independently selected from C_{2-6} alkenyl, C_{1-8} alkyl, C_{2-6} alkynyl or C_{3-6} cycloalkyl each optionally substituted with 1, 2, 3 or 4 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{2-8}

dialkylamino, C_{2-6} dialkylcarboxamide, C_{1-4} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, hydroxyl, hydroxylamino and nitro;

Ar_1 is aryl or heteroaryl each optionally substituted with R_{13}, R_{14}, R_{15}, R_{16}, and R_{17}; wherein R_{13} is selected from the group consisting of C_{1-5} acyl, C_{1-6} acylsulfonamide, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-6} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, arylsulfonyl, carbamimidoyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{3-7} cycloalkyloxy, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, guanidinyl, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heterocyclic, heterocyclic-oxy, heterocyclicsulfonyl, heterocyclic-carbonyl, heteroaryl, heteroarylcarbonyl, hydroxyl, nitro, C_{4-7} oxo-cycloalkyl, phenoxy, phenyl, sulfonamide, sulfonic acid, and thiol, and wherein said C_{1-5} acyl, C_{1-6} acylsulfonamide, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-6} alkylsulfonamide, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, arylsulfonyl, carbamimidoyl, C_{2-6} dialkylamino, heterocyclic, heterocyclic-carbonyl, heteroaryl, phenoxy and phenyl are optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-7} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{3-7} cycloalkyloxy, C_{2-6} dialkylamino, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heteroaryl, heterocyclic, hydroxyl, nitro, phenyl, and phosphonooxy, and wherein said C_{1-7} alkyl and C_{1-4} alkylcarboxamide are each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-4} alkoxy and hydroxy; or

R_{13} is a group of Formula (**IVA**):



(IVA)

wherein:

"p" and "r" are independently 0, 1, 2 or 3; and

R_{18} is H, C_{1-5} acyl, C_{2-6} alkenyl, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, heteroaryl or phenyl, and wherein said heteroaryl or phenyl optionally substituted with 1 to 5 substituents selected independently from the group consisting of C_{1-4} alkoxy,

amino, C_{1-4} alkylamino, C_{2-6} alkynyl, C_{2-8} dialkylamino, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl and hydroxyl;

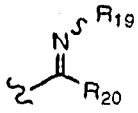
R_{14}, R_{15}, R_{16}, and R_{17} are each independently selected form the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{2-6} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-6} dialkylcarboxamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl and nitro; or

two adjacent R_{14}, R_{15}, R_{16} and R_{17} together with the atoms to which they are attached form a 5, 6 or 7 member cycloalkyl, cycloalkenyl or heterocyclic group fused with Ar_1 wherein the 5, 6 or 7 member group is optionally substituted with halogen; and

R_2 is selected from the group consisting of C_{1-8} alkyl, C_{2-6} alkynyl, amino, aryl, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, heteroaryl and hydroxyl; and wherein said C_{1-8} alkyl, aryl and heteroaryl are each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-3}-heteroalkylene, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heterocyclic, hydroxyl, hydroxylamino and nitro; or

R_2 is -Ar_2-Ar_3 wherein Ar_2 and Ar_3 are each independently aryl or heteroaryl each optionally substituted with 1 to 5 substituents selected from the group consisting of H, C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, amino, C_{1-4} alkylamino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-6}-cycloalkyl, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, halogen, hydroxyl and nitro; or

R_2 is a group of Formula (**IVB**):



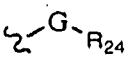
(IVB)

wherein:

R_{19} is H, C_{1-8} alkyl, C_{3-7} cycloalkyl, aryl, heteroaryl or OR_{21}; and R_{20} is F, Cl, Br, CN or $NR_{22}R_{23}$; where R_{21} is H, C_{1-8} alkyl or C_{3-7} cycloalkyl, and R_{22} and R_{23} are independently H, C_{1-8} alkyl, C_{3-7} cycloalkyl, aryl or heteroaryl;

or

R_2 is a group of Formula (IVC):



(IVC)

wherein:

G is:

i) -C(O)-, -C(O)NR_{25}-, -NR_{25}C(O)-, -NR_{25}-, -NR_{25}C(O)O-, -OC(O)NR_{25}-, -$CR_{25}R_{26}NR_{27}$C(O)-, -$CR_{25}R_{26}$C(O)NR_{27}-,-C(O)O-, -OC(O)-, -C(S)-, -C(S)NR_{25}-, -C(S)O-, -OC(S)-, -$CR_{25}R_{26}$-, -O-, -S-, -S(O)-, -$S(O)_2$- or a bond when D is CR_2R_3; or

ii) -$CR_{25}R_{26}$C(O)-, -C(O)-, -$CR_{25}R_{26}$C(O)NR_{27}-, -C(O)NR_{25}-, -C(O)O-, -C(S)-, -C(S)NR_{25}-, -C(S)O-, -$CR_{25}R_{26}$-, -$S(O)_2$-, or a bond when D is NR_2;

wherein R_{25}, R_{26} and R_{27} are each independently H or C_{1-8} alkyl; and R_{24} is H, C_{1-8} alkyl, C_{3-7} cycloalkyl, phenyl, heteroaryl, or heterocyclic each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{2-6} alkenyl, C_{1-4} alkoxy, C_{1-7} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heteroaryl, heterocyclic, hydroxyl, hydroxylamino, nitro, phenyl, phenoxy, and sulfonic acid, wherein said C_{1-4} alkoxy, C_{1-7} alkyl, C_{1-4} alkylamino, heteroaryl, phenyl and phenoxy are each optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-5} acyl, C_{1-5} acyloxy, C_{1-4} alkoxy, C_{1-8} alkyl, C_{1-4} alkylamino, C_{1-4} alkylcarboxamide, C_{1-4} alkylthiocarboxamide, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylthioureyl, C_{1-4} alkylureyl, amino, carbo-C_{1-6}-alkoxy, carboxamide, carboxy, cyano, C_{3-7} cycloalkyl, C_{2-8} dialkylamino, C_{2-6} dialkylcarboxamide, C_{2-6} dialkylthiocarboxamide, C_{2-6} dialkylsulfonamide, C_{1-4} alkylthioureyl, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkyl, C_{1-4} haloalkylthio, halogen, heterocyclic, hydroxyl, hydroxylamino, nitro, and phenyl;

provided that Z and U are not both N.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (**IV**) (referred to herein as **Group D1**): 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-3-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-3,6-dimethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isobutyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 1-(4-Methanesulfonyl-phenyl)-4-(piperidin-4-yloxy)-1H-pyrazolo[3,4-d]pyrimidine; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-pyridin-3-yl-methanone; (3-Fluoro-phenyl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (1-tert-Butyl-5-methyl-1H-pyrazol-4-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (5-tert-Butyl-2-methyl-2H-pyrazol-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidine-1-carboxylic acid isobutyl ester; Furan-2-yl-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(1-methyl-1H-pyrrol-2-yl)-methanone; 2-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-pyridin-3-yl-ethanone; 2-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-pyridin-2-yl-ethanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(5-methyl-pyridin-3-yl)-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(2-methyl-pyridin-3-yl)-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(6-methyl-pyridin-3-yl)-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(5-methyl-isoxazol-3-yl)-methanone; 2-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-thiophen-2-yl-ethanone; 4-(1-Benzyl-azetidin-3-yloxy)-1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidine; 3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidine-1-carboxylic acid tert-butyl ester; 1-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-3,3-dimethyl-butan-2-one; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-pyrazin-2-yl-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(5-methyl-pyrazin-2-yl)-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-pyrimidin-5-yl-methanone; {4-[1-(4-

Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-pyridazin-4-yl-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-thiophen-2-yl-methanone; (3,4-Dimethyl-isoxazol-5-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 3-tert-Butoxy-1-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-propan-1-one; (3-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-3-oxo-propyl)-methyl-carbamic acid tert-butyl ester; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(6-trifluoromethyl-pyridin-3-yl)-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexyl}-carbamic acid tert-butyl ester; N-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-cyclohexane-1,4-diamine; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(4-methyl-[1,2,3]thiadiazol-5-yl)-methanone; (3,5-Dimethyl-isoxazol-4-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (2,5-Dimethyl-2H-pyrazol-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(3-methyl-isoxazol-5-yl)-methanone; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carbothioic acid pyridin-4-ylamide; N-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexyl}-nicotinamide; 3-tert-Butoxy-N-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexyl}-propionamide; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexyl}-carbamic acid tert-butyl ester; (3,5-Dimethyl-isoxazol-4-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 4-[1-(3,5-Bis-trifluoromethyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-azetidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid propyl ester; 4-[1-(3-Fluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(2,4-Difluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; {4-[1-(2,4-Difluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexyl}-carbamic acid tert-butyl ester; {4-[1-(3-Fluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexyl}-carbamic acid tert-butyl ester; N-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-cyclohexane-1,4-diamine; {3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidin-1-yl}-(6-methyl-pyridin-3-yl)-methanone; {3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidin-1-yl}-(2-methyl-pyridin-3-yl)-methanone; {3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidin-1-yl}-(5-methyl-pyridin-3-yl)-methanone; {3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-

ylamino]-piperidin-1-yl}-pyridin-3-yl-methanone; {3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidin-1-yl}-(1-methyl-1H-pyrrol-3-yl)-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-cyclohexyl}-carbamic acid tert-butyl ester; N-[1-(2,4-Difluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-cyclohexane-1,4-diamine; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(4-trifluoromethyl-pyridin-3-yl)-methanone; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid cyclohexyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tetrahydro-pyran-4-yl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid cyclopentyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tetrahydro-furan-3-yl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tetrahydro-furan-3-yl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tetrahydro-thiopyran-4-yl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid cyclobutyl ester; (6-tert-Butyl-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (4-{[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-methyl}-cyclohexyl)-carbamic acid tert-butyl ester; N-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexylmethyl}-nicotinamide; N-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-cyclohexylmethyl}-6-methyl-nicotinamide; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-{[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-methyl}-piperidine-1-carboxylic acid tert-butyl ester; 3-{[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-methyl}-piperidine-1-carboxylic acid tert-butyl ester; 4-({Ethyl-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-{1-[2-(2-Dimethylamino-ethoxy)-4-methanesulfonyl-phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy}-piperidine-1-carboxylic acid tert-butyl ester; 3-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid pyridin-3-ylmethyl esteracid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 2-pyridin-3-yl-ethyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 3-pyridin-3-yl-propyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 2-dimethylamino-ethyl ester; 4-{[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-methyl-amino}-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(2,4-Difluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-

carboxylic acid tert-butyl ester; 4-({Ethyl-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; 4-({Ethyl-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-Dimethylamino-1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 1-(4-{[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-methyl-amino}-piperidin-1-yl)-3,3-dimethyl-butan-2-one; 4-{[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-methyl-amino}-piperidine-1-carboxylic acid cyclobutyl ester; and 4-[({1-[4-(2-Methanesulfonyl-ethyl)-phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (**IV**) (referred to herein as **Group D2**): 4-({[1-(2,5-Difluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 2-{4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-(4-trifluoromethoxy-phenyl)-ethanone; 2-{4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-(3-fluoro-phenyl)-ethanone; 2-{4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-pyridin-2-yl-ethanone; (2,5-Dimethyl-furan-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 4-({(2-Dimethylamino-ethyl)-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({(2-Dimethylamino-ethyl)-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(2-Dimethylamino-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-(2-{Ethyl-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-ethyl)-piperazine-1-carboxylic acid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-{2-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-ethyl}-piperazine-1-carboxylic acid ethyl ester; 4-{2-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-propyl}-piperazine-1-carboxylic acid ethyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4-sulfinyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4-sulfonyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid butyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid 2-methoxy-ethyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid 3,3-dimethyl-butyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-

carboxylic acid 4-methyl-pentyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid cyclopropylmethyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid cyclobutylmethyl ester; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid 2-cyclopropyl-ethyl ester; (5-Bromo-furan-2-yl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(5-morpholin-4-ylmethyl-furan-2-yl)-methanone; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid pentyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 1-ethyl-propyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 2-ethyl-butyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid cyclopentylmethyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 2-pyrrolidin-1-yl-ethyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 2-morpholin-4-yl-ethyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid ethyl ester; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 2,2-dimethyl-propyl ester; (5-Butyl-pyridin-2-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; Ethyl-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-(3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-ylmethyl)-amine; Ethyl-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-(5'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-ylmethyl)-amine; [1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-(5'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-yl)-amine; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 5'-Fluoro-4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-5'-methyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-6'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; [1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-[1-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-pyrrolidin-3-yl]-amine; [1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-[1-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-pyrrolidin-3-yl]-amine; (4-Ethyl-pyridin-2-yl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 1-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-pyrrolidin-3-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; (5'-Fluoro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl;-4-yl)-[1-(4-

methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine; (5-Bromo-pyridin-3-yl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 3-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-pyrrolidine-1-carboxylic acid tert-butyl ester; 3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester; 3-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid isopropyl ester; (6-Chloro-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (5-Chloro-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(1-methyl-3-trifluoromethyl-1H-pyrazol-4-yl)-methanone; (2-Chloro-pyridin-4-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (4-Hydroxy-3-methoxy-phenyl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (4-Chloro-3-nitro-phenyl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 1-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-3-methyl-butan-1-one; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(6-pyrazol-1-yl-pyridin-3-yl)-methanone; (2-Hydroxy-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (5,6-Dichloro-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (5-Bromo-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 5-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carbonyl}-nicotinic acid; (1H-Imidazol-4-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 3-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-pyrrolidine-1-carboxylic acid tert-butyl ester; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(6-pyrrolidin-1-yl-pyridin-3-yl)-methanone; (6-Isobutylamino-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (6-Ethylamino-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (6-Cyclobutylamino-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (6-Isopropylamino-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; [6-(1-Ethyl-propylamino)-pyridin-3-yl]-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-[6-(1-propyl-butylamino)-pyridin-3-yl]-methanone; 5-Benzyloxy-2-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carbonyl}-pyran-4-one; Benzo[c]isoxazol-3-yl-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-

piperidin-1-yl}-methanone; (4-Chloro-pyridin-2-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (4-Iodo-pyridin-2-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 1-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-butan-2-one; 2-(5-Bromo-pyridin-3-yl)-1-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; (6-Fluoro-pyridin-2-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (5-Fluoro-pyridin-2-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (6-Chloro-pyridin-2-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (2-Chloro-5-fluoro-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-[5-(2-methyl-pyrrolidin-1-ylmethyl)-pyridin-3-yl]-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(6-methyl-pyridin-2-yl)-methanone; 5-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carbonyl}-nicotinonitrile; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(4-methoxy-pyridin-2-yl)-methanone; (2-Fluoro-pyridin-4-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (2-Fluoro-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (6-Fluoro-pyridin-3-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(4-methoxy-thiophen-3-yl)-methanone; 2-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carbonyl}-pyran-4-one; (5-Ethyl-pyridin-2-yl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (4-Ethoxy-phenyl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(5-pyridin-2-yl-thiophen-2-yl)-methanone; (5-Amino-pyridin-2-yl)-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (5-Amino-pyridin-2-yl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-[5-(3-methyl-butylamino)-pyridin-2-yl]-methanone; {4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(4-trifluoromethoxy-phenyl)-methanone; (5-Butyl-pyridin-2-yl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (5-Ethylamino-pyridin-2-yl)-{4-[1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(5-isopropoxymethyl-pyridin-2-yl)-methanone; (4-Difluoromethoxy-phenyl)-{4-[1-(2-

fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(5-isopropoxy-pyridin-2-yl)-methanone; 5-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carbonyl}-pyridine-2-carboxylic acid methyl ester; {4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-acetic acid ethyl ester; {4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-(3-trifluoromethoxy-phenyl)-methanone; 1-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(4-Chloro-phenyl)-2-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 2-{4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-(3-trifluoromethyl-phenyl)-ethanone; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-5'-isopropoxy-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 1-(4-Methanesulfonyl-phenyl)-4-[1-(4-trifluoromethoxy-phenyl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(4-trifluoromethoxy-phenyl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(4-Chloro-3-methyl-phenyl)-2-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(3,4-Dichloro-phenyl)-2-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 5'-Bromo-4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 1-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(3-trifluoromethoxy-phenyl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-5'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 1-(2,4-Dimethoxy-phenyl)-2-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(4-Difluoromethoxy-phenyl)-2-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; 1-(4-Diethylamino-phenyl)-2-{4-[1-(4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-ethanone; (2-{4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-5-methyl-pyrimidin-4-yl)-dimethyl-amine; 1-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(5-methyl-4-pyrrolidin-1-yl-pyrimidin-2-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2-Methyl-4-propylamino-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Isopropylamino-2-methyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2-Methyl-4-morpholin-4-yl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{1-[4-(2-Methoxy-ethylamino)-2-methyl-phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(1-{4-[(2-Methanesulfonyl-ethyl)-methyl-amino]-2-methyl-phenyl}-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Bromo-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-

carboxylic acid isopropyl ester; 4-[1-(4-Propylamino-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Isopropylamino-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-(1-{4-[4-(2-Methanesulfonyl-ethyl)-piperazin-1-yl]-2-methyl-phenyl}-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-(1-{2-Methyl-4-[(tetrahydro-furan-2-ylmethyl)-amino]-phenyl}-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Cyclopropylamino-2-methyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{1-[4-(2-Dimethylamino-ethylamino)-2-methyl-phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Morpholin-4-yl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-({[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-isopropyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[1-(2-Fluoro-4-morpholin-4-yl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2-Fluoro-4-isopropylamino-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-(1-{4-[(2-Methanesulfonyl-ethyl)-methyl-amino]-phenyl}-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{1-[4-(2-Methoxy-ethylamino)-phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(1-{4-[(Tetrahydro-furan-2-ylmethyl)-amino]-phenyl}-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-(1-{4-[4-(2-Methanesulfonyl-ethyl)-piperazin-1-yl]-phenyl}-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Amino-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-({[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-isopropyl-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(5-Ethyl-pyrimidin-2-yl)-piperidin-4-ylsulfanyl]-1-(2-fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidine; 4-[1-(2-Fluoro-4-sulfamoyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2-Fluoro-4-propionylsulfamoyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Cyano-2-fluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 1-(2,5-Difluoro-4-methoxy-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1H-pyrazolo[3,4-d]pyrimidine; 4-[1-(2,5-Difluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Fluoro-6-methoxy-pyridin-3-yl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(6-Methoxy-2-methyl-pyridin-3-yl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2,5-Difluoro-4-sulfamoyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2-Fluoro-4-hydroxy-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{4-[1-(3-

isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-benzonitrile; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-benzenesulfonamide; 1-(2,5-Difluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(4-Fluoro-6-methoxy-pyridin-3-yl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 4-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-(6-methoxy-2-methyl-pyridin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine; 2,5-Difluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-benzenesulfonamide; 1-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1H-pyrazolo[3,4-d]pyrimidine; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-benzonitrile; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-benzenesulfonamide; 1-(2,5-Difluoro-4-methanesulfonyl-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(4-Fluoro-6-methoxy-pyridin-3-yl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1H-pyrazolo[3,4-d]pyrimidine; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-(6-methoxy-2-methyl-pyridin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine; 2,5-Difluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-benzenesulfonamide; 4-[1-(2-Fluoro-4-methoxy-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(4-Difluoromethoxy-2-fluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2-Fluoro-4-trifluoromethoxy-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[1-(2,5-Difluoro-4-methoxy-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-phenol; 1-(2-Fluoro-4-methoxy-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(4-Difluoromethoxy-2-fluoro-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(2-Fluoro-4-trifluoromethoxy-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(2,5-Difluoro-4-methoxy-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1H-pyrazolo[3,4-d]pyrimidine; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[3,4-d]pyrimidin-1-yl}-phenol; 1-(2-Fluoro-4-methoxy-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1H-pyrazolo[3,4-d]pyrimidine; 1-(4-Difluoromethoxy-2-fluoro-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1H-pyrazolo[3,4-d]pyrimidine; and 1-(2-Fluoro-4-trifluoromethoxy-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1H-pyrazolo[3,4-d]pyrimidine.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (IV) (referred to herein as **Group D3**): 4-[9-(6-Methanesulfonyl-pyridin-3-yl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isobutyl ester; {4-[9-(6-Methanesulfonyl-pyridin-3-yl)-9H-purin-6-yloxy]-piperidin-1-yl}-pyridin-3-yl-methanone; 4-[9-(4-Methanesulfonyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[9-(6-Methanesulfonyl-pyridin-3-yl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid tert-butyl ester and 4-[9-(2-Fluoro-4-methanesulfonyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid tert-butyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (IV) (referred to herein as **Group D4**): 4-[9-(2-Fluoro-4-propionylsulfamoyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[9-(4-Cyano-2-fluoro-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[9-(2-Fluoro-4-sulfamoyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 9-(2-Fluoro-4-methanesulfonyl-phenyl)-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-9H-purine; 3-Fluoro-4-{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-purin-9-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-purin-9-yl}-benzonitrile; 3-Fluoro-4-{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-purin-9-yl}-benzenesulfonamide; 4-[9-(2,5-Difluoro-4-methanesulfonyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[9-(4-Fluoro-6-methoxy-pyridin-3-yl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[9-(6-Methoxy-2-methyl-pyridin-3-yl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[9-(2,5-Difluoro-4-sulfamoyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 9-(2,5-Difluoro-4-methanesulfonyl-phenyl)-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-9H-purine; 9-(4-Fluoro-6-methoxy-pyridin-3-yl)-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-9H-purine; 6-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-9-(6-methoxy-2-methyl-pyridin-3-yl)-9H-purine; 2,5-Difluoro-4-{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-purin-9-yl}-benzenesulfonamide; 9-(2-Fluoro-4-methanesulfonyl-phenyl)-6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-9H-purine; 3-Fluoro-4-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-purin-9-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-purin-9-yl}-benzonitrile; 3-Fluoro-4-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-purin-9-yl}-benzenesulfonamide; 9-(2,5-Difluoro-4-methanesulfonyl-phenyl)-6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-9H-purine; 9-(4-Fluoro-6-methoxy-pyridin-3-yl)-6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-9H-purine; 6-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-9-(6-methoxy-2-methyl-pyridin-3-yl)-9H-purine; and 2,5-Difluoro-4-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-purin-9-yl}-benzenesulfonamide.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compound according to Formula (IV) (referred to herein as **Group D5**): 4-[3-(4-Methanesulfonyl-phenyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid tert-butyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (IV) (referred to herein as **Group D6**): 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3H-[1,2,3]triazolo[4,5-d]pyrimidine; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-3H-[1,2,3]triazolo[4,5-d]pyrimidine; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-3H-[1,2,3]triazolo[4,5-d]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-3H-[1,2,3]triazolo[4,5-d]pyrimidine; 7-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine; 2,5-Difluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-benzenesulfonamide; 4-[3-(2-Fluoro-4-methanesulfonyl-phenyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-propionylsulfamoyl-phenyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Cyano-2-fluoro-phenyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-sulfamoyl-phenyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Fluoro-6-methoxy-pyridin-3-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(6-Methoxy-2-methyl-pyridin-3-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-sulfamoyl-phenyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3H-[1,2,3]triazolo[4,5-d]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3H-

[1,2,3]triazolo[4,5-d]pyrimidine; 7-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine; and 2,5-Difluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-benzenesulfonamide.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compound according to Formula (IV) (referred to herein as **Group D7**): 4-[3-(4-Methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid tert-butyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (IV) (referred to herein as **Group D8**): 4-({Ethyl-[3-(4-methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[3-(4-Methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-ylsulfanyl]-piperidine-1-carboxylic acid tert-butyl ester; and 4-[3-(4-Methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compound according to Formula (IV) (referred to herein as **Group D9**): 4-[8-(2-Fluoro-4-methanesulfonyl-phenyl)-[1,7]naphthyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (IV) (referred to herein as **Group D10**): 4-[8-(2-Fluoro-4-methanesulfonyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Methylsulfanyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Methanesulfonyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Isopropoxy-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Bromo-2-fluoro-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2-Fluoro-4-propionylsulfamoyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Cyano-2-fluoro-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2-Fluoro-4-sulfamoyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2,5-Difluoro-4-methanesulfonyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Fluoro-6-methoxy-pyridin-3-yl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(6-Methoxy-2-methyl-pyridin-3-yl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2,5-Difluoro-4-sulfamoyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 2,5-Difluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-quinolin-8-yl}-benzenesulfonamide; 4-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-8-(6-methoxy-2-methyl-pyridin-3-yl)-quinoline; 8-(4-Fluoro-6-methoxy-pyridin-3-yl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-quinoline; 8-(2,5-Difluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-

piperidin-4-yloxy]-quinoline; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-quinolin-8-yl}-benzenesulfonamide; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-quinolin-8-yl}-benzonitrile; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-quinolin-8-yl}-N-propionyl-benzenesulfonamide; 8-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-quinoline; 2,5-Difluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-quinolin-8-yl}-benzenesulfonamide; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-8-(6-methoxy-2-methyl-pyridin-3-yl)-quinoline; 8-(4-Fluoro-6-methoxy-pyridin-3-yl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-quinoline; 8-(2,5-Difluoro-4-methanesulfonyl-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-quinoline; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-quinolin-8-yl}-benzenesulfonamide; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-quinolin-8-yl}-benzonitrile; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-quinolin-8-yl}-N-propionyl-benzenesulfonamide; and 8-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-quinoline.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (**IV**) (referred to herein as **Group D11**): 4-[8-(2-Fluoro-4-methanesulfonyl-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2-Fluoro-4-propionylsulfamoyl-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Cyano-2-fluoro-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2-Fluoro-4-sulfamoyl-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2,5-Difluoro-4-methanesulfonyl-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(4-Fluoro-6-methoxy-pyridin-3-yl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(6-Methoxy-2-methyl-pyridin-3-yl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[8-(2,5-Difluoro-4-sulfamoyl-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 8-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrido[3,4-d]pyrimidine; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrido[3,4-d]pyrimidin-8-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrido[3,4-d]pyrimidin-8-yl}-benzonitrile; 3-Fluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrido[3,4-d]pyrimidin-8-yl}-benzenesulfonamide; 8-(2,5-Difluoro-4-methanesulfonyl-phenyl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrido[3,4-d]pyrimidine; 8-(4-Fluoro-6-methoxy-pyridin-3-yl)-4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrido[3,4-d]pyrimidine; 4-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-8-(6-methoxy-2-methyl-pyridin-3-yl)-pyrido[3,4-d]pyrimidine; 2,5-Difluoro-4-{4-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrido[3,4-d]pyrimidin-8-yl}-benzenesulfonamide; 8-(2-Fluoro-4-methanesulfonyl-phenyl)-4-[4-(3-

isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrido[3,4-d]pyrimidine; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrido[3,4-d]pyrimidin-8-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrido[3,4-d]pyrimidin-8-yl}-benzonitrile; 3-Fluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrido[3,4-d]pyrimidin-8-yl}-benzenesulfonamide; 8-(2,5-Difluoro-4-methanesulfonyl-phenyl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrido[3,4-d]pyrimidine; 8-(4-Fluoro-6-methoxy-pyridin-3-yl)-4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrido[3,4-d]pyrimidine; 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-8-(6-methoxy-2-methyl-pyridin-3-yl)-pyrido[3,4-d]pyrimidine; and 2,5-Difluoro-4-{4-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrido[3,4-d]pyrimidin-8-yl}-benzenesulfonamide.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (**IV**) (referred to herein as **Group D12**): 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidine; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidine; 7-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-pyrazolo[1,5-a]pyrimidine; 2,5-Difluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide; 4-[3-(2-Fluoro-4-methanesulfonyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-propionylsulfamoyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Cyano-2-fluoro-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-sulfamoyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Fluoro-6-methoxy-pyridin-3-yl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(6-Methoxy-2-methyl-pyridin-3-yl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-sulfamoyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[1,5-a]pyrimidine; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-

piperidin-4-yloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[1,5-a]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[1,5-a]pyrimidine; 7-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-pyrazolo[1,5-a]pyrimidine; 2,5-Difluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide; 4-[3-(2-Fluoro-4-methanesulfonyl-phenyl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-propionylsulfamoyl-phenyl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Cyano-2-fluoro-phenyl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-sulfamoyl-phenyl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Fluoro-6-methoxy-pyridin-3-yl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(6-Methoxy-2-methyl-pyridin-3-yl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-sulfamoyl-phenyl)-2-methyl-pyrazolo[1,5-a]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 2,5-Difluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide; 7-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-2-methyl-pyrazolo[1,5-a]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-pyrazolo[1,5-a]pyrimidine; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-pyrazolo[1,5-a]pyrimidine; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-pyrazolo[1,5-a]pyrimidine; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-pyrazolo[1,5-a]pyrimidine; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-pyrazolo[1,5-a]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-pyrazolo[1,5-a]pyrimidine; 7-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-

cyclohexyloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-2-methyl-pyrazolo[1,5-a]pyrimidine; and 2,5-Difluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-pyrazolo[1,5-a]pyrimidin-3-yl}-benzenesulfonamide.

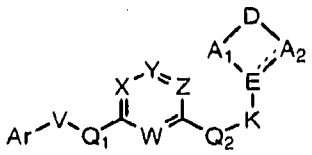
Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include include the following compounds according to Formula (**IV**) (referred to herein as **Group D13**): 4-[3-(2-Fluoro-4-methanesulfonyl-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-propionylsulfamoyl-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Cyano-2-fluoro-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-sulfamoyl-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Fluoro-6-methoxy-pyridin-3-yl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(6-Methoxy-2-methyl-pyridin-3-yl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-sulfamoyl-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; 7-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; 2,5-Difluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; 7-[4-(3-Isopropyl-

[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidine; and 2,5-Difluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2004/022417 include the following compounds according to Formula (IV) (referred to herein as **Group D14**): 4-[3-(2-Fluoro-4-methanesulfonyl-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-propionylsulfamoyl-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Cyano-2-fluoro-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2-Fluoro-4-sulfamoyl-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(4-Fluoro-6-methoxy-pyridin-3-yl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(6-Methoxy-2-methyl-pyridin-3-yl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-(2,5-Difluoro-4-sulfamoyl-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidine; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidine; 7-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidine; 2,5-Difluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidine; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzonitrile; 3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide; 3-(2,5-Difluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidine; 3-(4-Fluoro-6-methoxy-pyridin-3-yl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidine; 7-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-3-(6-methoxy-2-methyl-pyridin-3-yl)-2-

methyl-2H-pyrazolo[4,3-d]pyrimidine; and 2,5-Difluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-3-yl}-benzenesulfonamide.

Examples of GPR119 agonists are described in International Application No. PCT/US2005/019318 (published as WO 2005/121121), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US2005/019318 as a GPR119 agonist is a compound of Formula (V):



(V)

or N-oxide thereof;

wherein:

A_1 and A_2 are independently C_{1-3} alkylene optionally substituted with one or more substituents selected independently from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, and carboxy;

D is CR_1R_2 or NR_2, wherein R_1 is selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} alkoxy, halogen and hydroxyl;

E is N, C or CR_3, wherein R_3 is H or C_{1-6} alkyl;

--- is a single bond when E is N or CR_3, or a double bond when E is C;

K is absent, C_{3-6} cycloalkylene, or C_{1-3} alkylene group optionally substituted with one or more substituents selected independently from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, carboxy, cyano, and halogen;

Q_1 is NR_4, O, S, S(O) or $S(O)_2$, wherein R_4 is H, C_{1-6} acyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, or C_{3-7}-cycloalkyl-C_{1-3}-alkylene, wherein said C_{1-6} alkyl is optionally substituted with one or more substituents selected independently from the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, hydroxylamino and nitro;

Q_2 is absent, NR_5, or O, wherein R_5 is H, C_{1-6} acyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, or C_{3-7}-cycloalkyl-C_{1-3}-alkylene, wherein said C_{1-6} alkyl is optionally substituted with one or more substituents selected independently from the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6}

alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, hydroxylamino and nitro;

W is N or CH;

X is N or CR_6;

Y is N or CR_7;

Z is N or CR_8;

V is absent, C_{1-3} heteroalkylene, or C_{1-3} alkylene wherein each are optionally substituted with one or more substituents selected independently from the group consisting of C_{1-3} alkyl, C_{1-6} alkoxy, carboxy, cyano, C_{1-3} haloalkyl, and halogen;

R_6, R_7, and R_8 are each independently selected from the group consisting of H, C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, hydroxylamino and nitro, wherein said C_{2-6} alkenyl, C_{1-6} alkyl, C_{2-6} alkynyl and C_{3-6} cycloalkyl are each optionally substituted with one or more substituents independently selected from the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, hydroxylamino and nitro;

Ar is aryl or heteroaryl optionally substituted with R_9-R_{13};

R_9 is selected from the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, aryl, arylcarbonyl, arylsulfonyl, di-C_{1-6}-alkylamino, carbamimidoyl, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, guanidine, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heterocyclic, heterocyclicsulfonyl, heteroaryl, hydroxyl, hydroxylamino, nitro, C_{3-6} oxo-cycloalkyl, phenoxy, sulfonamide, sulfonic acid and thiol; and wherein each available R_9 is optionally substituted with one or more substituents selected independently from the group

consisting of C_{1-6} acyl, C_{1-6} acylsulfonamide, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, aryl, arylcarbonyl, arylsulfonyl, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heteroaryl, heteroarylcarbonyl, heteroarylsulfonyl, heterocyclic, hydroxyl, hydroxylamino, and nitro;

R_{10}-R_{13} are independently selected from the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, hydroxyl, hydroxylamino, nitro, and thiol; or two adjacent groups together with the atoms to which they are bonded form a 5, 6 or 7 member cycloalkyl, cycloalkenyl or heterocyclic group wherein the 5, 6 or 7 member group is optionally substituted with halogen or oxo; and

R_2 is selected from the group consisting of H, C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, aryl, arylcarbonyl, aryloxy, di-C_{1-6}-alkylamino, carbamimidoyl, C_{1-6} alkoxycarbonyl, C_{3-7}-cycloalkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, guanidine, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heteroaryl, heteroaryl-C_{1-3}-alkylene, heteroarylcarbonyl, heteroaryloxy, heterocycliccarboxamide, hydroxyl, hydroxylamino and nitro; wherein each available R_2 is optionally substituted with one or more substituents selected independently from the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkylcarboxamide, C_{2-6} alkynyl, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylthiocarboxamide, C_{1-6} alkylthioureyl, C_{1-6} alkylureyl, amino, aryl, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, di-C_{1-6}-alkylthiocarboxamido, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heterocyclic, heteroaryl, hydroxyl, hydroxylamino and nitro, and wherein C_{1-6} alkyl is further optionally substituted with one or more substituents selected independently from the group consisting of C_{1-6} acyl, C_{1-6} alkoxy, C_{1-6} alkylamino, C_{1-6}

alkylcarboxamide, C_{1-6} alkylsulfonamide, C_{1-6} alkylsulfinyl; C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, amino, di-C_{1-6}-alkylamino, C_{1-6} alkoxycarbonyl, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, di-C_{1-6}-alkylcarboxamide, di-C_{1-6}-alkylsulfonamide, C_{1-6} haloalkoxy, C_{1-6} haloalkyl, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6} haloalkylthio, heterocyclic, hydroxyl, hydroxylamino and nitro.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2005/019318 include the following compounds according to Formula (V) (referred to herein as **Group E1**): 4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methanesulfonyl-phenoxy)-pyrimidine; {6-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine; 4-{[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,5-Difluoro-benzylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[({6-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-fluoro-phenoxy)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 4-({Methyl-[6-(2-pyridin-4-yl-ethylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(2-pyridin-3-yl-ethylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[(Methyl-{6-[(pyridin-3-ylmethyl)-amino]-pyrimidin-4-yl}-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-[({6-[(2-Fluoro-4-methanesulfonyl-phenyl)-methyl-amino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; 4-({[6-(4-Cyano-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[({6-[4-(2-Methanesulfonyl-ethyl)-phenylamino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Ethylsulfanyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Isopropylsulfanyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Ethylsulfamoyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(4-methylsulfamoyl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Dimethylsulfamoyl-

phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(4-methylsulfamoylmethyl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(4-sulfamoyl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(4-[1,2,4]triazol-1-yl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(4-[1,2,4]triazol-1-ylmethyl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[(Methyl-{6-[4-(2-[1,2,4]triazol-1-yl-ethyl)-phenylamino]-pyrimidin-4-yl}-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(Benzo[1,3]dioxol-5-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(6-Methanesulfonyl-pyridin-3-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(3,5-Dimethoxy-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[(Methyl-{6-[4-(2-oxo-oxazolidin-4-ylmethyl)-phenylamino]-pyrimidin-4-yl}-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-[({6-[4-(1,1-Dioxo-1λ6-thiomorpholin-4-ylmethyl)-phenylamino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(4-pyrazol-1-yl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,2-Difluoro-benzo[1,3]dioxol-5-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(4-trifluoromethanesulfonyl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[(Methyl-{6-[4-(morpholine-4-sulfonyl)-phenylamino]-pyrimidin-4-yl}-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-[(Methyl-{6-[2-(pyridine-2-carbonyl)-phenylamino]-pyrimidin-4-yl}-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-5-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; N-Ethyl-3-fluoro-4-[6-(methyl-piperidin-4-ylmethyl-amino)-pyrimidin-4-ylamino]-benzenesulfonamide; 3-Fluoro-N-isopropyl-4-[6-(methyl-piperidin-4-ylmethyl-amino)-pyrimidin-4-ylamino]-benzenesulfonamide; 4-({[6-(3,4-Difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,6-Difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,5-Difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,3-Difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(2,3,5-trifluoro-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-4-methyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(3-Chloro-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,4-Difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[(Methyl-{6-[2-(1-oxy-pyridin-3-yl)-

ethylamino]-pyrimidin-4-yl}-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-[(Methyl-{6-[2-(1-oxy-pyridin-3-yl)-ethylamino]-pyrimidin-4-yl}-amino)-methyl]-piperidine-1-carboxylic acid isobutyl ester; 4-({[6-(2,5-Difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; 4-({[6-(4-Cyano-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; 4-[({6-[2-(2-Fluoro-phenoxy)-ethylamino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-phenoxy)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,5-Difluoro-phenoxy)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[({6-[2-(2-Chloro-phenoxy)-ethylamino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Chloro-phenoxy)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[({6-[2-(4-Fluoro-phenoxy)-propylamino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Ethylsulfamoyl-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-4-isopropylsulfamoyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Cyano-2,5-difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Bromo-2,5-difluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(5-Carboxy-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(6-Methoxy-pyridin-3-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,6-Dimethoxy-pyridin-3-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 6-{6-[(1-tert-Butoxycarbonyl-piperidin-4-ylmethyl)-methyl-amino]-pyrimidin-4-ylamino}-nicotinic acid; 4-({[6-(6-Acetylamino-pyridin-3-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(5-Fluoro-pyridin-2-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Cyano-2-ethyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Butyryl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(5-Bromo-3-methyl-pyridin-2-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(3-Bromo-5-methyl-pyridin-2-ylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Methyl-[6-(5-trifluoromethyl-pyridin-2-ylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Bromo-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(3-Carboxy-4-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(4-Ethoxycarbonyl-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; 4-({[6-(4-Carboxy-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-

1-carboxylic acid isobutyl ester; 4-({[6-(4-Cyano-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; 4-({[6-(4-Cyano-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid butyl ester; 4-({[6-(4-Cyano-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid cyclopropylmethyl ester; {4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-piperazin-1-yl}-acetic acid ethyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-piperazin-1-yl]-pyrimidin-4-yl}-amine; 4-({[6-(2,5-Difluoro-4-hydroxy-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; 4-({[6-(4-Ethylcarbamoyl-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; 4-[({6-[2-Fluoro-4-(N-hydroxycarbamimidoyl)-phenylamino]-pyrimidin-4-yl}-methyl-amino)-methyl]-piperidine-1-carboxylic acid isobutyl ester; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid 3-methyl-butyl ester; 4-({[6-(2,5-Difluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; (5-Butyl-pyridin-2-yl)-[4-({[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidin-1-yl]-methanone; N-(2-Fluoro-4-methanesulfonyl-phenyl)-N'-(5'-fluoro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-ylmethyl)-N'-methyl-pyrimidine;-4,6-diamine; 4-({[6-(4-Carbamimidoyl-2-fluoro-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid cyclobutyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-ylamino]-piperidine-1-carboxylic acid tert-butyl ester; N-(2-Fluoro-4-methanesulfonyl-phenyl)-N'-[1-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-piperidin-4-ylmethyl]-N'-methyl-pyrimidine;-4,6-diamine; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid 1-ethyl-propyl ester; 4-({Ethyl-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Ethyl-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; 4-({[6-(4-Cyano-2,5-difluoro-phenylamino)-pyrimidin-4-yl]-ethyl-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester; 4-({[6-(4-Amino-2,5-difluoro-phenoxy)-pyrimidin-4-yl]-ethyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,5-Difluoro-4-methoxy-phenylamino)-pyrimidin-4-yl]-ethyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[6-(2,5-Difluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-ethyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({Ethyl-[6-(2,4,5-trifluoro-phenylamino)-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 4-[(Ethyl-{6-[4-(N-ethylcarbamimidoyl)-2,5-difluoro-phenylamino]-pyrimidin-4-yl}-amino)-methyl]-

piperidine-1-carboxylic acid isopropyl ester; 4-({[6-(4-Bromo-2,5-difluoro-phenylamino)-pyrimidin-4-yl]-ethyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-[({6-[5-(2-Amino-ethylamino)-4-cyano-2-fluoro-phenylamino]-pyrimidin-4-yl}-ethyl-amino)-methyl]-piperidine-1-carboxylic acid isopropyl ester; {1-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-piperidin-4-yl}-acetic acid methyl ester; 3-{4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-piperazin-1-yl}-propionic acid ethyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(4-isobutyl-phenyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(4-isopropyl-phenyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; {6-[4-(3-Cyclopropylmethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-(2-fluoro-4-methanesulfonyl-phenyl)-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isobutyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(4-isopropoxy-phenyl)-piperazin-1-yl]-pyrimidin-4-yl}-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(4-isopropoxy-phenyl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(5-isopropoxy-pyridin-2-yl)-piperazin-1-yl]-pyrimidin-4-yl}-amine; {6-[4-(3-Dimethylaminomethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-(2-fluoro-4-methanesulfonyl-phenyl)-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-(6-{4-[2-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-ethyl]-piperazin-1-yl}-pyrimidin-4-yl)-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(5-isopropoxy-pyridin-2-yloxy)-piperidin-1-yl]-pyrimidin-4-yl}-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-pyridin-3-yl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-amine; 2,5-Difluoro-4-{6-[4-(4-isopropoxy-phenyl)-piperazin-1-yl]-pyrimidin-4-ylamino}-benzonitrile; 4-{[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-ylamino]-methyl}-piperidine-1-carboxylic acid tert-butyl ester; 4-{[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-ylamino]-methyl}-piperidine-1-carboxylic acid isopropyl ester; 4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-isopropyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester; 4-({[4-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyridin-2-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester; and 4-({[2-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyridin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid isobutyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US2005/019318 include the following compounds according to Formula (V) (referred to herein as **Group E2**): 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-piperidin-4-yloxy]-pyrimidin-4-yl}-amine; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; (6-Chloro-pyridin-2-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; (6-Bromo-pyridin-2-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-(6-methyl-pyridin-2-yl)-methanone; {4-[6-(2-Fluoro-4-

methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-(6-fluoro-pyridin-2-yl)-methanone; {4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-pyridin-2-yl-methanone; (5-Bromo-pyridin-3-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; {4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-(5-methyl-pyridin-3-yl)-methanone; (5,6-Dichloro-pyridin-3-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 4-[6-(4-Cyano-2,5-difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2,5-Difluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2,4,5-Trifluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(4-Bromo-2,5-difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(3-Fluoro-4-methyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(3-Hydroxy-4-methoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Cyano-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(3-Chloro-4-cyano-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Chloro-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(3-Fluoro-4-methoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(3,4-Dimethoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2,3-Dihydro-benzo[1,4]dioxin-6-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(4-Cyano-2,5-difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Cyano-5-ethylamino-2-fluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(4-Ethoxy-2,5-difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Ethylsulfanyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(4-Isopropylsulfanyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; (5-Butyl-pyridin-2-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone; 4-[6-(5-Chloro-3-methyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Acetylamino-4-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(5-Fluoro-4-methyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Methoxy-5-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Methoxy-2-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Fluoro-5-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Chloro-6-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(4-Methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Chloro-2-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Fluoro-pyridin-3-

ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Chloro-4-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Methoxy-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(5-Fluoro-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Fluoro-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(6-Chloro-5-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Methyl-pyridin-4-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Methoxy-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2,5-Difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(4-Chloro-2-fluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2,5-Difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methoxy-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Cyano-3-methoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3-Fluoro-4-hydroxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Ethoxy-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-isopropoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-[6-(5'-isopropoxy-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-yloxy)-pyrimidin-4-yl]-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrimidin-4-yl}-amine; 4-[6-(4-Cyano-2-fluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(Pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(Pyridin-4-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-propoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Ethylamino-2-fluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Dimethylamino-2-fluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-propylamino-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-isopropylamino-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Methyl-6-propylamino-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Isopropylamino-2-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Methyl-6-propoxy-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Iodo-2-methyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-iodo-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[Methyl-(2-methyl-4,5,6,7-tetrahydro-2H-indazol-3-yl)-amino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Methyl-2H-pyrazol-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Phenyl-

2H-pyrazol-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-tert-Butyl-1H-pyrazol-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-p-Tolyl-1H-pyrazol-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methoxy-5-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Acetylamino-3-methyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3-Chloro-4-fluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3,5-Dimethoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Ethyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Methyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Methyl-quinolin-6-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Methylsulfanyl-benzothiazol-6-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Morpholin-4-yl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Benzenesulfonyl-thiophen-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Piperidin-1-yl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3-Trifluoromethoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Oxo-5,6,7,8-tetrahydro-naphthalen-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methyl-1H-pyrazolo[3,4-b]pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Cyano-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Bromo-2,5-difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Trifluoromethyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Methyl-1H-pyrazol-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Cyclopropyl-1H-pyrazol-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,6-Dimethyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Cyano-2-methyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Methoxy-2-methyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,4-Dimethoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[Acetyl-(2-fluoro-4-methanesulfonyl-phenyl)-amino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Carbamoyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-(3,4-Difluoro-phenyl)-thiazol-2-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Oxo-1-phenyl-4,5-dihydro-1H-pyrazol-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3-Oxazol-5-yl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Trifluoromethyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Chloro-2-trifluoromethoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid

isopropyl ester; 4-{6-[(5-Pyridin-2-yl-thiophen-2-ylmethyl)-amino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[5-(4-Chloro-phenyl)-2H-pyrazol-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(1-Oxo-indan-5-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[5-(1-Methyl-pyrrolidin-2-yl)-pyridin-2-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methoxy-2-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(5-Bromo-3-methyl-pyridin-2-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Chloro-6-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Ethynyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Bromo-2-trifluoromethoxy-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3-Iodo-4-methyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-5-methyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[5-(4-Methoxy-phenyl)-[1,3,4]thiadiazol-2-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(3,5-Dimethyl-isoxazol-4-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2,5-Difluoro-4-propoxy-phenylamino)-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-propylamino-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-4-morpholin-4-yl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Methyl-4-propylamino-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(4-methyl-piperazin-1-yl)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-pyrrolidin-1-yl-ethoxy)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[4-(2-Dimethylamino-ethoxy)-2,5-difluoro-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-morpholin-4-yl-ethoxy)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,4-Difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,4,5-Trifluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[Acetyl-(4-methanesulfonyl-phenyl)-amino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; (2,5-Difluoro-4-propoxy-phenyl)-{6-[1-(5-isopropyl-[1,2,4]oxadiazol-3-yl)-piperidin-4-yloxy]-pyrimidin-4-yl}-amine; 4-{6-[2,5-Difluoro-4-(morpholin-4-ylamino)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-methoxy-ethylamino)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2,5-Difluoro-4-[(tetrahydro-furan-2-ylmethyl)-amino]-phenylamino}-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Butylamino-2,5-difluoro-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(3-methyl-butylamino)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-

phenylamino)-2-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(2-morpholin-4-yl-ethylamino)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-(2,5-Difluoro-phenoxy)-ethylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2,5-Difluoro-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Bromo-2-fluoro-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-morpholin-4-yl-phenoxy)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2,5-Difluoro-4-(tetrahydro-furan-2-ylmethoxy)-phenylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyridin-2-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[5-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyridin-3-yloxy]-piperidine-1-carboxylic acid tert-butyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyridin-2-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[4-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyridin-2-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[4-(2,5-Difluoro-4-propoxy-phenylamino)-pyridin-2-yloxy]-piperidine-1-carboxylic acid isopropyl ester; and 4-[2-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2,5-Difluoro-4-propoxy-phenylamino)-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester.

Examples of GPR119 agonists are described in International Application No. PCT/GB2004/050046 (published as WO 2005/061489), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/GB2004/050046 as a GPR119 agonist is a compound of Formula (VI):

$$R^1\text{-}A\text{-}V\text{-}B\text{-}R^2$$

(VI)

wherein:

V is a 5-membered heteroaryl ring containing up to four heteroatoms selected from O, N and S, optionally substituted by C_{1-4} alkyl;

A is –CH=CH– or $(CH_2)_n$;

B is –CH=CH– or $(CH_2)_n$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$, C(O) or $C(O)NR^{12}$;

n is independently 0, 1, 2 or 3;

m is independently 0, 1 or 2;

R^1 is 3- or 4-pyridyl, 4- or 5-pyrimidinyl or 2-pyrazinyl, any of which may be optionally substituted by one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, a 4- to 7-membered heterocyclyl group or a 5- or 6-membered heteroaryl group;

R^2 is 4- to 7-membered cycloalkyl substituted by R^3, $C(O)OR^3$, $C(O)R^3$ or $S(O)_2R^3$, or 4- to 7-membered heterocyclyl, containing one or two nitrogen atoms which is unsubstituted or

substituted by $C(O)OR^4$, $C(O)R^3$, $S(O)_2R^3$, $C(O)NHR^4$, $P(O)(OR^{11})_2$ or a 5- or 6-membered nitrogen containing heteroaryl group;

R^3 is C_{3-8} alkyl, C_{3-8} alkenyl or C_{3-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is hydrogen, $C(O)R^7$, $S(O)_2R^8$, C_{3-7} cycloalkyl or C_{1-4} alkyl optionally substituted by OR^6, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-2} alkyl, C_{1-2} fluoroalkyl, OR^6, CN, $N(R^6)_2$ and NO_2;

R^6 are independently hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $(N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^7 is hydrogen, C_{1-4} alkyl, OR^6, $N(R^6)_2$, aryl or heteroaryl;

R^8 is C_{1-4} alkyl, C_{1-4} fluoroalkyl, aryl or heteroaryl;

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;

R^{10} is hydrogen or C_{1-4} alkyl;

R^{11} is phenyl; and

R^{12} is hydrogen, C_{1-4} alkyl or C_{3-7} cycloalkyl.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/GB2004/050046 include the following compounds according to Formula (**VI**) (referred to herein as **Group F1**): 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid *tert*-

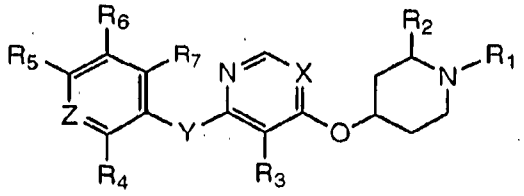
butyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid *tert*-butyl ester; 3-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Pentylcyclohexylmethyl)-[1,2,4]oxadiazol-3-yl]pyridine; *trans*-2-Chloro-4-[5-(4-pentylcyclohexane)-[1,2,4]oxadiazol-3-yl]pyridine; *trans*-4-[5-(4-Pentylcyclohexane)-[1,2,4]oxadiazol-3-ylmethyl]pyridine; 4-(3-Pyridin-4-ylmethyl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid *tert*-butyl ester; *trans*-3-[5-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-3-ylmethyl]pyridine; 4-[5-(4-Butylcyclohexane)-[1,2,4]oxadiazol-3-yl]pyridine; 4-[5-(4-*n*-Propylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine; *trans*-4-[5-(4-Pentylcyclohexane)-[1,2,4]oxadiazol-3-yl]pyridine; 4-[2-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)-ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 3-[5-(4-Propylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine; 3-[5-(4-Butylcyclohexane)-[1,2,4]oxadiazol-3-yl]pyridine; *trans*-4-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine-2-carboxylic acid methylamide; *trans*-4-[5-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine-2-carboxylic acid amide; *trans*-4-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Chloro-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-3-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Methyl-3-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Chloro-6-methyl-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-4-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine-2-carbonitrile; *trans*-2-Chloro-3-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Chloro-6-methyl-3-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Methyl-5-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-3-Methyl-5-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2,6-Dichloro-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Chloro-6-methoxy-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-5-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]-2-[1,2,4]triazol-1-ylpyridine; 2-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyrazine; 4-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyrimidine; *trans*-5-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine-2-carbonitrile; *trans*-5-Chloro-2-methylsulfanyl-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyrimidine; *trans*-2-Fluoro-5-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Fluoro-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Imidazol-1-yl-5-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-2-Methyl-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-3-Methyl-4-[3-(4-pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]pyridine; *trans*-4-{2-[3-(4-Pentylcyclohexyl)-[1,2,4]oxadiazol-5-yl]vinyl}pyridine; 4-(5-Pyridin-4-yl-[1,2,4]oxadiazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(2-Cyanopyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-[5-(2-Pyridin-3-yl-vinyl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-[5-(2-Pyridin-3-yl-vinyl)-[1,2,4]oxadiazol-3-yl]piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-[5-(2-Pyridin-3-yl-vinyl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-[5-(2-Pyridin-4-yl-

vinyl)-[1,2,4]oxadiazol-3-yl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(2-Pyridin-4-yl-ethyl)-[1,2,4]oxadiazol-3-yl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-{5-[2-(2-Cyanopyridin-4-yl)ethyl]-[1,2,4]oxadiazol-3-yl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-{5-[2-(2-Cyanopyridin-4-yl)ethyl]-[1,2,4]oxadiazol-3-ylmethoxy}piperidine-1-carboxylic acid *tert*-butyl ester; 4-{5-[2-(2-Cyanopyridin-4-yl)ethyl]-[1,2,4]oxadiazol-3-ylmethyl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Piperidin-4-yl-[1,2,4]oxadiazol-3-yl)pyridine; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid isobutyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid 2-methoxyethyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid ethyl ester; 3,3-Dimethyl-1-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidin-1-yl]butan-1-one; 2-Cyclopentyl-1-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidin-1-yl]ethanone; 4-{5-[1-(Butane-1-sulfonyl)piperidin-4-yl]-[1,2,4]oxadiazol-3-yl}pyridine; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid propylamide; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid *tert*-butylamide; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid cyclopentyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid benzyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid isobutyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid ethyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid cycloheptyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid methyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 2-methoxy-ethyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid isopropyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 4-methoxy-phenyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 2,2,2-trichloroethyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 4-chloro-phenyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid phenyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 2-ethyl-hexyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid propyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid hexyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid (*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid (*1S,2R,5S*)-2-isopropyl-5-methylcyclohexyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 2,2-dimethylpropyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid naphthalen-1-yl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 2-methoxy-phenyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 3-trifluoromethylphenyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid prop-2-ynyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid but-2-ynyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid pentyl ester; 4-(3-Pyridin-4-yl-

[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid *p*-tolyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 2-chloro-phenyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid naphthalen-2-yl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid butyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 4-methoxycarbonyl-phenyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 4-fluoro-phenyl ester; 3-Methyl-1-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]-butan-1-one; Phenyl-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]methanone; 1-[4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]butan-1-one; 2,2-Dimethyl-1-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]propan-1-one; Cyclopentyl-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]methanone; [4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]-*p*-tolylmethanone; 3,3-Dimethyl-1-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]butan-1-one; 4-{5-[1-(Butane-1-sulfonyl) piperidin-4-yloxymethyl]-[1,2,4]oxadiazol-3-yl}pyridine; 4-{5-[1-(Propane-1-sulfonyl) piperidin-4-yloxymethyl]-[1,2,4]oxadiazol-3-yl}pyridine; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid *tert*-butylamide; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid *o*-tolylamide; *trans*-4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)cyclohexanecarboxylic acid propyl ester; *trans*-4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)cyclohexanecarboxylic acid butyl ester; *trans*-4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-yl)cyclohexanecarboxylic acid isobutyl ester; *trans*-4-[5-(4-Propoxymethylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine; *trans*-4-[5-(4-Butoxymethylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine; *cis*-4-[5-(3-Butoxymethylcyclopentyl)-[1,2,4]oxadiazol-3-yl]pyridine; *cis*-4-[5-(3-Propoxymethylcyclopentyl)-[1,2,4]oxadiazol-3-yl]pyridine; *cis*-4-[5-(3-Butoxymethylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)-3,4,5,6-tetrahydro-2H-[1,3']bipyridinyl; 2-[4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]pyrazine; 2-[4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]pyrimidine; (4-Pentylcyclohexyl)-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amine; (4-Pentylcyclohexyl-methyl)-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amine; 4-[(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-{[3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]methyl}-piperidine-1-carboxylic acid *tert*-butyl ester; 4-{[5-(2-Cyanopyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethyl]amino}-piperidine-1-carboxylic acid *tert*-butyl ester; Methyl-(4-pentylcyclohexyl)-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amine; Methyl-(4-pentylcyclohexylmethyl)-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amine; 4-[Methyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Ethyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Propyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Cyclopropylmethyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Butyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-

ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-{[Methyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]methyl}-piperidine-1-carboxylic acid *tert*-butyl ester; 4-{[Ethyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]methyl}-piperidine-1-carboxylic acid *tert*-butyl ester; 4-{[5-(2-Cyanopyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethyl]ethylamino}-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Methyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid cyclopentyl ester; 4-{[Methyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]methyl}-piperidine-1-carboxylic acid 2,2,2-trichloroethyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxymethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)piperazine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethanesulfonyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Pyridin-4-yl-[1,3,4]oxadiazol-2-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 3-Pyridin-4-yl-[1,2,4]oxadiazole-5-carboxylic acid (4-pentylcyclohexyl)amide; [4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidin-1-yl]phosphonic acid diphenyl ester; 4-(4-Pyridin-4-yl-thiazol-2-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-yl-thiazol-4-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; *trans*-4-[5-(4-Pentyl-cyclohexyl)-[1,3,4]thiadiazol-2-yl]pyridine; 4-(5-Pyridin-4-yl-[1,3,4]thiadiazol-2-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Pyridin-4-yl-4H-[1,2,4]triazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(5-Pyridin-4-yl-isoxazol-3-yl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Pyridin-4-yl-isoxazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Pyridin-4-yl-isoxazol-3-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(1-Methyl-5-pyridin-4-yl-1H-pyrazol-3-yl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(2-Methyl-5-pyridin-4-yl-2H-pyrazol-3-yl)ethyl]-piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-{5-[2-(2-Cyanopyridin-4-yl)vinyl]-[1,2,4]oxadiazol-3-yl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-{5-[2-(2H-Tetrazol-5-yl)pyridine-4-yl]-[1,2,4]oxadiazol-3-ylmethoxy}-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(2-Cyanopyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid isopropyl ester; and 4-[5-(2-Cyanopyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid phenyl ester.

Examples of GPR119 agonists are described in International Application No. PCT/US06/00567 (published as WO 2006/083491), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US06/00567 as a GPR119 agonist is a compound of Formula (**VII**):



(**VII**)

wherein:

X is N or CR_8 wherein R_8 is H or halogen;

Y is NH or O;

Z is CH or N;

R_1 is carbo-C_{1-6}-alkoxy, oxadiazolyl or pyrimidinyl wherein said carbo-C_{1-6}-alkoxy, oxadiazolyl and pyrimidinyl are each optionally substituted with 1 or 2 substituents selected independently from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy and C_{3-5} cycloalkyl;

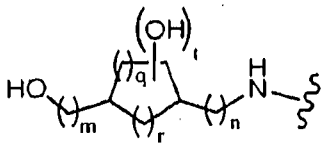
R_2 is H or C_{1-4} alkyl;

R_3 is C_{1-4} alkoxy, O-C_{2-4}-alkynyl or hydroxyl;

R_4 is selected from the group consisting of H, C_{1-4} alkoxy, C_{1-4} alkyl, C_{2-4} alkynyl and halogen;

R_5 is selected from the group consisting of C_{1-4} acylsulfonamide, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} alkylamino, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, cyano, heterocyclyl, di-C_{1-4}-dialkylamino and sulfonamide, wherein said C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} alkylamino, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, di-C_{1-4}-dialkylamino and heterocyclyl are each optionally substituted with 1 or 2 substituents selected independently from the group consisting of C_{2-4} alkynyl, C_{1-4} alkoxy, C_{1-4} alkylcarboxamide, C_{1-4} alkylsulfonyl, C_{3-5} cycloalkyl, C_{3-5} cycloalkyloxy, di-C_{1-4}-alkylcarboxamide, hydroxyl and phosphonooxy, wherein said C_{1-4} alkylcarboxamide is optionally substituted with hydroxyl; or

R_5 is a group of Formula (**VIIA**):



(VIIA)

wherein "m", "n" and "q" are each independently 0, 1, 2 or 3; "r" is 0, 1 or 2; and "t" is 0 or 1;

R_6 is H or halogen; and

R_7 is H or C_{1-4} alkyl.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US06/00567 include the following compounds according to Formula (**VII**) (referred to herein as **Group G1**): 4-[6-(4-Methanesulfonyl-2-methoxy-phenylamino)-5-methoxy-pyrimidin-4-yloxy]-

piperidine-1-carboxylic acid isopropyl ester; 4-{5-Methoxy-6-[6-(2-methoxy-ethyl)-2-methyl-pyridin-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methanesulfonyl-ethyl)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid 1-cyclopropyl-ethyl ester; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(4-Cyano-2-fluoro-phenylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Hydroxy-ethyl)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methanesulfonyl-ethyl)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Methoxy-6-[6-(2-methoxy-ethylamino)-2-methyl-pyridin-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methanesulfonyl-ethoxy)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Hydroxy-propylamino)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(3-Hydroxy-propyl)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Methoxy-6-[2-methyl-6-(3-phosphonooxy-propyl)-pyridin-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methanesulfonyl-ethylamino)-2-methoxy-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methanesulfonyl-propylamino)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Dimethylcarbamoylmethyl-2-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-(6-{2-Fluoro-4-[(2-hydroxy-ethylcarbamoyl)-methyl]-phenylamino}-5-methoxy-pyrimidin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Methanesulfonyl-ethylamino)-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[2-Fluoro-4-(2-hydroxy-ethylsulfanyl)-phenylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2,3-Dihydroxy-propylamino)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2,3-Dihydroxy-propylamino)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Hydroxy-ethoxy)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Methoxy-6-[2-methyl-6-(2-phosphonooxy-ethoxy)-pyridin-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(3-Hydroxy-propoxy)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; and 4-{5-Methoxy-6-[2-methyl-6-(3-phosphonooxy-propoxy)-pyridin-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US06/00567 include the following compounds according to Formula (VII) (referred to herein as **Group G2**): 4-[2-(2-Fluoro-4-propoxy-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-

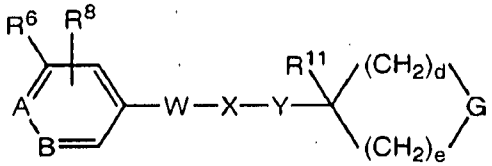
carboxylic acid isopropyl ester; 4-{2-[2-Fluoro-4-(2-hydroxy-ethyl)-phenylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Fluoro-2-(2-fluoro-4-methanesulfonyl-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2-Ethyl-4-(2-methanesulfonyl-ethyl)-phenylamino]-3-methoxy-pyridin-4-yloxy}-2-methyl-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Fluoro-2-[6-(2-hydroxy-ethoxy)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2-Fluoro-4-(2-methanesulfonyl-ethyl)-phenylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Hydroxy-ethylamino)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(4-Cyano-2-fluoro-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2-Chloro-4-cyano-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Methanesulfonyl-ethyl)-2-methoxy-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Methanesulfonyl-ethyl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Hydroxy-ethyl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(3-Hydroxy-butyl)-2-methoxy-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2-Fluoro-4-(2-hydroxy-ethoxy)-phenylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{3-Ethoxy-2-[2-fluoro-4-(2-phosphonooxy-ethyl)-phenylamino]-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[3-Methoxy-2-(2-methoxy-4-propionylsulfamoyl-phenylamino)-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2,5-Difluoro-4-propoxy-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; (2-Fluoro-4-methanesulfonyl-phenyl)-{4-[1-(5-isopropyl-[1,2,4]oxadiazol-3-yl)-piperidin-4-yloxy]-3-methoxy-pyridin-2-yl}-amine; (2-Fluoro-4-methanesulfonyl-phenyl)-{3-methoxy-4-[1-(5-methoxy-pyrimidin-2-yl)-piperidin-4-yloxy]-pyridin-2-yl}-amine; 4-{2-[6-(2-Cyclopropoxy-ethyl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2-Chloro-4-methanesulfonyl-phenylamino)-5-fluoro-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[3-Ethoxy-2-(4-methanesulfonyl-2-methoxy-phenylamino)-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(5-Fluoro-2-methyl-4-propoxy-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Methanesulfonyl-ethyl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2-Fluoro-4-methanesulfonyl-phenylamino)-3-hydroxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(2-Chloro-4-propoxy-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{3-Methoxy-2-[2-methyl-6-(2-phosphonooxy-ethyl)-pyridin-3-ylamino]-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Methanesulfonyl-ethylamino)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-(2-{6-[(2-Methanesulfonyl-ethyl)-methyl-amino]-2-methyl-pyridin-3-ylamino}-3-methoxy-pyridin-4-yloxy)-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(3-

Methanesulfonyl-pyrrolidin-1-yl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(3-Methanesulfonyl-6'-methyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-ylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(3-Methanesulfonyl-azetidin-1-yl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[3-Ethynyloxy-2-(2-fluoro-4-methanesulfonyl-phenylamino)-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2-Fluoro-4-(2-phosphonooxy-ethanesulfonyl)-phenylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[2-(4-Ethanesulfonyl-2-fluoro-phenylamino)-3-methoxy-pyridin-4-yloxy]-piperidine-1-carboxylic acid sec-butyl ester; 4-{2-[6-(2,3-Dihydroxy-propylamino)-4-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Hydroxy-ethylsulfanyl)-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2-Fluoro-4-(2-hydroxy-ethanesulfonyl)-phenylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Hydroxy-ethoxy)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{3-Methoxy-2-[2-methyl-6-(2-phosphonooxy-ethoxy)-pyridin-3-ylamino]-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(3-Hydroxy-propoxy)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{3-Methoxy-2-[2-methyl-6-(3-phosphonooxy-propoxy)-pyridin-3-ylamino]-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[3-Methoxy-2-(2-methoxy-4-sulfamoyl-phenylamino)-pyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[2-Fluoro-4-(3-phosphonooxy-propyl)-phenylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(2-Hydroxy-ethyl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{3-Methoxy-2-[2-methyl-6-(2-phosphonooxy-ethyl)-pyridin-3-ylamino]-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{2-[6-(3-Hydroxy-propyl)-2-methyl-pyridin-3-ylamino]-3-methoxy-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; and 4-{3-Methoxy-2-[2-methyl-6-(3-phosphonooxy-propyl)-pyridin-3-ylamino]-pyridin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/US06/00567 include the following compounds according to Formula (**VII**) (referred to herein as **Group G3**): 4-[6-(2,6-Dimethyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methanesulfonyl-2-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methanesulfonyl-4-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Methoxy-6-(2-methyl-6-propylsulfanyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Methoxy-6-[2-methyl-6-(propane-1-sulfonyl)-pyridin-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Ethylsulfanyl-2-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Ethanesulfonyl-2-

methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Isopropylsulfanyl-2-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-{5-Methoxy-6-[2-methyl-6-(propane-2-sulfonyl)-pyridin-3-ylamino]-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-{6-[6-(2-Hydroxy-ethanesulfonyl)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Hydroxy-6-(6-methanesulfonyl-2-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Ethoxy-6-(6-methanesulfonyl-2-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[5-Isopropoxy-6-(6-methanesulfonyl-2-methyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methanesulfonyl-2-methyl-pyridin-3-ylamino)-5-propoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Methanesulfonyl-2-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid 1-ethyl-propyl ester; 4-[6-(6-Methanesulfonyl-2-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid sec-butyl ester; 4-[6-(6-Cyano-4-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; 4-[6-(6-Hydroxymethyl-4-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; {6-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-5-methoxy-pyrimidin-4-yl}-(6-methanesulfonyl-2-methyl-pyridin-3-yl)-amine; 4-[6-(6-Methanesulfonyl-2,4-dimethyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester; and 4-{6-[6-(1-Methanesulfonyl-1-methyl-ethyl)-2-methyl-pyridin-3-ylamino]-5-methoxy-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl.

Examples of GPR119 agonists are described in International Application No. PCT/GB2005/050264 (published as WO 2006/067531), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/GB2005/050264 as a GPR119 agonist is a compound of Formula **(VIII)**:



(VIII)

wherein:

one of A and B is nitrogen and the other is CR^1;

W and Y are independently a bond, an unbranched or a branched C_{1-3} alkylene or an unbranched or a branched C_{2-3} alkenylene;

X is selected from CH_2, O, S, CH(OH), CH(halogen), C(O), C(O)O, C(O)S, SC(O), $C(O)CH_2S$, $C(O)CH_2C(OH)$, $C(O)CH_2C(O)$, OC(O), NR^5, $CH(NR^5R^{55})$, $C(O)NR^2$, S(O) and $S(O)_2$;

G is CHR^3, N-$C(O)OR^4$, N-$C(O)NR^4R^5$, N-C_{1-4}alkylene-$C(O)OR^4$, N-$C(O)C(O)OR^4$, N-$S(O)_2R^4$, N-$C(O)R^4$ or N-$P(O)(O\text{-}Ph)_2$; or N-heterocyclyl or N-heteroaryl, either of which may optionally be substituted by one or two groups selected from C_{1-4}alkyl, C_{1-4}alkoxy or halogen;

R^1 is hydrogen, halogen, cyano, $C(O)NH_2$, C_{1-4}alkyl, SO_2C_{1-4}alkyl, SOC_{1-4}alkyl or SC_{1-4}alkyl;

R^2 is hydrogen or C_{1-4}alkyl;

R^3 is C_{3-6}alkyl;

R^4 is C_{1-8}alkyl, C_{2-8}alkenyl or C_{2-8}alkynyl, any of which may be optionally substituted by one or more halo atoms, NR^5R^{55}, OR^5, $C(O)OR^5$, $OC(O)R^5$ or cyano, and may contain a CH_2 group that is replaced by O or S; or a C_{3-7}cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4}alkyleneC_{3-7}cycloalkyl, C_{1-4}alkylenearyl, C_{1-4}alkyleneheterocyclyl or C_{1-4}alkyleneheteroaryl, any of which may be substituted with one or more substitutents selected from halo, C_{1-4}alkyl, C_{1-4}fluoroalkyl, OR^5, CN, NR^5R^{55}, SO_2Me, NO_2 or $C(O)OR^5$;

R^5 and R^{55} are independently hydrogen or C_{1-4}alkyl; or taken together R^5 and R^{55} may form a 5 or 6 membered heterocyclic ring;

R^6 is hydrogen, halogen, CN, C_{1-4}alkyl, C_{1-4}alkoxy, ethynyl, $C(O)NR^7R^{77}$ or C_{1-4}alkylene$S(O)_f$;

R^7 and R^{77} are independently hydrogen or C_{1-4}alkyl; or taken together R^7 and R^{77} may form a 5 or 6 membered heterocyclic ring;

R^8 is hydrogen, halogen, CN, C_{1-4}alkyl or C_{1-4}alkoxy;

R^{11} is hydrogen or hydroxy;

d is 0, 1, 2 or 3;

e is 1, 2, 3, 4 or 5;

with the proviso that d + e is 2, 3, 4 or 5; and

f is 0, 1 or 2.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

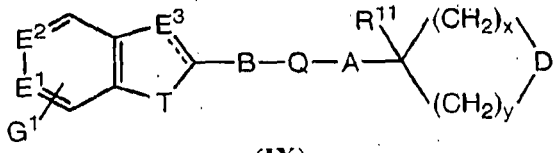
Specific examples of GPR119 agonists disclosed in International Application No. PCT/GB2005/050264 include the following compounds according to Formula (**VIII**) (referred to herein as **Group H1**): 4-(3-Pyridin-4-ylpropylsulfanylcarbonyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-Pentylcyclohexane carbothioic acid *S*-(3-pyridin-4-ylpropyl) ester; 4-(2-Pyridin-4-ylethylsulfanylcarbonyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-Pentylcyclohexane carbothioic acid *S*-(2-pyridin-4-ylethyl) ester; 4-(Pyridine-4-carbonylsulfanyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-(3-Pyridin-4-ylacryloylsulfanyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-

Pyridin-4-ylpropionylsulfanyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(Pyridine-4-carbonylsulfanylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropionylsulfanylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-ylacetoxymethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-ylacetoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[3-(2-Pyridin-4-ylacetoxy)propyl]piperidine-1-carboxylic acid *tert*-butyl ester; Isonicotinic acid 3-(1-*tert*-butoxycarbonylpiperidin-4-yl)propyl ester; (*E*)-4-(3-Pyridin-4-ylacryloyloxymethyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-(3-Pyridin-4-ylacryloyloxy)piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-[3-(3-Pyridin-4-ylacryloyloxy)propyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-ylethoxycarbonylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; Piperidine-1,4-dicarboxylic acid 1-*tert*-butyl ester 4-(2-pyridin-4-ylethyl) ester; Piperidine-1,4-dicarboxylic acid 1-*tert*-butyl ester 4-(3-pyridin-4-ylpropyl) ester; (*E*)-4-[Methyl(3-pyridin-4-ylacryloyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-{2-[Methyl(pyridine-4-carbonyl)amino]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Methyl(pyridine-4-carbonyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-{2-[Methyl(2-pyridin-4-ylacetyl)amino]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-{2-[Methyl(3-pyridin-4-ylacryloyl)amino]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-{[Methyl-(3-pyridin-4-ylacryloyl)amino]methyl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-ylethylsulfanylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-ylethylsulfanyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(2-Pyridin-4-ylethylsulfanyl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropylsulfanylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropylsulfanyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(3-Pyridin-4-ylpropylsulfanyl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-ylethoxymethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropoxymethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(3-Pyridin-4-ylpropoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(2-Pyridin-4-ylethoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[3-(2-Cyanopyridin-4-yl)propoxymethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-{2-[3-(2-Cyanopyridin-4-yl)propoxy]ethyl}piperidine-1-carboxylic acid *tert*-butyl ester; 4-[3-Pyridin-4-ylmethoxy)propyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(2-Bromopyridin-4-ylmethoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[3-(pyridin-4-yloxy)propyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(Pyridin-4-ylmethoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Oxo-2-pyridin-4-ylethylsulfanylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropane-1-sulfonyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropane-1-sulfinyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropane-1-sulfonylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropane-1-sulfinylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester;

4-[2-(3-Pyridin-4-ylpropane-1-sulfonyl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(3-Pyridin-4-ylpropane-1-sulfinyl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Pyridin-4-ylethanesulfonylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-(2-Oxo-4-pyridin-4-ylbut-3-enyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-(4-Pyridin-4-ylbut-3-enyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*Z*)-4-(4-Pyridin-4-ylbut-3-enyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-(3-Pyridin-4-ylallyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*Z*)-4-(3-Pyridin-4-ylallyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Pyridin-4-ylpropyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Methyl-3-pyridin-4-ylpropyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*E*)-4-[4-(2-Cyanopyridin-4-yl)but-3-enyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)butyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[3-(2-Cyanopyridin-4-yl)propyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(2-Cyanopyridin-4-ylmethoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butylamide; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butylmethylamide; 4-(4-Pyridin-4-yl-butyl)piperidine-1-carboxylic acid 2,2,2-trichloroethyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid isobutyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 4-methoxyphenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 2,2-dimethylpropyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid phenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid cyclopentyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 2-chlorobenzyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid *p*-tolyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid propyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid hexyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid prop-2-ynyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid naphthalen-1-yl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 4-fluorophenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 4-methoxycarbonylphenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 4-nitrophenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid isopropyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 4-chlorophenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 3-trifluoromethylphenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 2-chlorophenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 2-methoxyphenyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid but-2-ynyl ester, 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid naphthalen-2-yl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid pentyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid *o*-tolyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 2-cyano-1,1-dimethylethyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 2,2,2-trifluoroethyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid cyclobutyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid cyclohexyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid 2-methylsufanylethyl ester; 4-(4-Pyridin-4-ylbutyl)piperidine-1-carboxylic acid tetrahydrofuran-2-ylmethyl ester; 2-[4-(4-Pyridin-4-ylbutyl)piperidin-1-yl]propionic acid ethyl ester; [4-(4-Pyridin-4-ylbutyl)piperidin-1-yl]acetic acid ethyl ester; [4-(4-Pyridin-4-ylbutyl)piperidin-1-yl]acetic acid *tert*-butyl

ester; Oxo-[4-(4-pyridin-4-ylbutyl)piperidin-1-yl]acetic acid methyl ester; 2-[4-(4-Pyridin-4-ylbutyl)piperidin-1-yl]pyrimidine; 4-(4-Pyridin-4-ylbutyl)-3,4,5,6-tetrahydro-2*H*-[1,2']bipyridinyl; 4-(2,4-Dioxo-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3,5-Dioxo-5-pyridin-4-yl-pentyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[1-(2-Cyanopyridin-4-yl)vinyloxycarbonylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Hydroxy-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Hydroxy-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Hydroxy-4-oxo-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-2-hydroxy-4-oxobutyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(1-Hydroxy-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; (*Z*)-4-(4-Oxo-4-pyridin-4-ylbut-2-enyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(4-Oxo-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(4-hydroxy-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-2-hydroxybutyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-4-hydroxybutyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-1-hydroxybutyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Oxo-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Oxo-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(4-Pyridin-4-yl-butyryl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-2-oxobutyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)butyryl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)butyryl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Methylamino-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(1-Methylamino-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-4-methylaminobutyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyano-pyridin-4-yl)-2-methylamino-butyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(1-Dimethylamino-4-pyridin-4-ylbutyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-4-dimethylaminobutyl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Cyanopyridin-4-yl)-2-dimethylaminobutyl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(2-Carbamoylpyridin-4-ylmethoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(2-Ethynylpyridin-4-ylmethoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[(*E*)-4-(2-Methylpyridin-4-yl)but-3-enyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[(*Z*)-4-(2-Methylpyridin-4-yl)but-3-enyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(2-Methylpyridin-4-yl)butyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-Hydroxy-4-[4-(2-methylpyridin-4-yl)butyl]piperidine-1-carboxylic acid *tert*-butyl ester.

Examples of GPR119 agonists are described in International Application No. PCT/GB2005/050265 (published as WO 2006/067532), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/GB2005/050265 as a GPR119 agonist is a compound of Formula (**IX**):



(IX)

or an N-oxide thereof,

wherein:

one of E^1 and E^2 is N and the other is N or C-G^2;

the dashed line together with the solid line forms an optional double bond;

when the dashed line together with the solid line forms a double bond E^3 is CR^8 or N, and when it is a single bond E^3 is CHR^8, O or NR^2;

T is O, S, NR^2, $(CH_2)_2$, or E^4=E^5, where E^4 and E^5 are independently CH or N;

B is a bond, -CH_2=CH_2- or $(CH_2)_j$;

j is 1, 2 or 3;

Q is a bond, C(O)S, or a 5- or 6-membered heteroaromatic ring;

A is $(CH_2)_n$, where one CH_2 group may be replaced by O, S, C(O), CH(OH) CH(Hal) $CH(NR^2R^3)$, S(O), $S(O)_2$ or NR^3; two CH_2 groups may be replaced by CH=CH, C(O)O, C(O)S, SC(O), $C(O)NR^2$ or OC(O); or three CH_2 groups may be replaced by $C(O)CH_2S$, $C(O)CH_2C(OH)$ or $C(O)CH_2C(O)$;

n is 0, 1, 2, 3, 4, 5, or 6;

G^1 and G^2 are independently hydrogen, halogen, CF_3, C_{1-4}alkoxy, NR^4R^{44}, SO_2C_{1-4}alkyl, SOC_{1-4}alkyl, SC_{1-4}alkyl or cyano; or C_{1-4}alkyl, C_{2-4}alkenyl, or C_{2-4}alkynyl, optionally substituted by hydroxy, NR^4R^{44}, oxo or C_{1-4}alkoxy;

D represents CHR^9 or NR^1;

R^1 is $C(O)OR^5$, $C(O)R^5$, $S(O)_2R^5$, $C(O)NR^5R^{10}$, $C(O)NR^5R^{55}$, C_{1-4}alkylene-$C(O)OR^5$, $C(O)C(O)OR^5$, $S(O)_2R^5$, $C(O)R^5$ or $P(O)(O\text{-}Ph)_2$; or heterocyclyl or heteroaryl, either of which may optionally be substituted by one or two groups selected from C_{1-4}alkyl, C_{1-4}alkoxy, C_{1-4}alkyl-OH, halogen, C_{1-4}fluoroalkyl, heterocyclyl, $C(O)OC_{1-4}$alkyl;

R^2 and R^3 are independently hydrogen or C_{1-4}alkyl;

R^4 and R^{44} are independently hydrogen, C_{1-4}alkyl, C_{3-7}cycloalkyl, or aryl, which may optionally be substituted with 1 or 2 substituents selected from halo, C_{1-4}alkyl, CF_3, C_{1-4}alkoxy, cyano, and $S(O)_2Me$; or, taken together, R^4 and R^{44} may form a 5- or 6-membered heterocyclic ring;

R^5 and R^{55} are independently C_{1-8}alkyl, C_{2-8}alkenyl or C_{2-8}alkynyl, any of which may be optionally substituted by one or more halo atoms, NR^6R^{66}, OR^6, $C(O)OR^6$, $OC(O)R^6$ or cyano, and may contain a CH_2 group that is replaced by O or S; or a C_{3-7}cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4}alkyleneC_{3-7}cycloalkyl, C_{1-4}alkylenearyl, C_{1-4}alkyleneheterocyclyl or C_1.

$_{4}$alkyleneheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4}alkyl, C_{1-4}fluoroalkyl, OR^7, CN, NR^7R^{77}, SO_2Me, NO_2 or $C(O)OR^7$;

R^6, R^{66}, R^7, and R^{77} each independently are hydrogen or C_{1-4}alkyl; or, taken together, R^6 and R^{66} or R^7 and R^{77} may form a 5- or 6-membered heterocyclic ring;

R^8 is hydrogen, hydroxy, C_{1-4}alkoxy or benzyloxy;

R^9 is C_{3-6}alkyl

R^{10} is hydrogen or C_{1-4}alkyl;

R^{11} is hydrogen or hydroxy;

x is 0, 1, 2 or 3; and

y is 1, 2, 3, 4 or 5;

with the proviso that x + y is 2, 3, 4 or 5.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/GB2005/050265 include the following compounds according to Formula (IX) (referred to herein as **Group I1**): 4-(Furo[3,2-c]pyridine-2-carbonylsulfanyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-([1,6]Naphthyridine-2-carbonylsulfanyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-([1,7]Naphthyridine-3-carbonylsulfanyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(6-Chloro-1*H*-pyrrolo[3,2-c]pyridine-2-carbonylsulfanyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(1*H*-Pyrrolo[2,3-c]pyridine-2-carbonylsulfanyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Chloro-1*H*-pyrrolo[2,3-c]pyridine-2-carbonylsulfanyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-([1,6]Naphthyridine-2-carbonylsulfanylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(1*H*-Pyrrolo[2,3-c]pyridine-2-carbonylsulfanylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(Furo[3,2-c]pyridine-2-carbonylsulfanylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(6-Chloro-1*H*-pyrrolo[3,2-c]pyridine-2-carbonylsulfanylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Chloro-1*H*-pyrrolo[2,3-c]pyridine-2-carbonylsulfanylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-([1,7]Naphthyridine-3-carbonylsulfanylmethyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(Furo[3,2-c]pyridin-2-ylmethoxy)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(Furo[3,2-c]pyridin-2-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(Furo[3,2-c]pyridin-2-ylmethoxymethyl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[3-(Furo[3,2-c]pyridin-2-ylmethoxy)propyl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[4-(Furo[3,2-c]pyridin-2-ylmethoxy)butyl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Furo[3,2-c]pyridin-2-ylethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Furo[3,2-c]pyridin-2-ylpropyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Furo[2,3-c]pyridin-2-ylethyl)piperidine-1-carboxylic acid *tert*-

butyl ester; 4-(2-Oxazolo[4,5-c]pyridin-2-yl-2-oxo-ethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Chloro-2-oxazolo[4,5-c]pyridin-2-ylethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(2-Oxazolo[4,5-c]pyridin-2-yl-ethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Hydroxymethylfuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Methoxymethylfuro[3,2-c]pyridine-2-yl)-[1,2,4]oxadiazole-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Dimethylaminomethylfuro[3,2-c]pyridine-2-yl)-[1,2,4]oxadiazole-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Pyrrolidin-1-ylmethylfuro[3,2-c]pyridine-2-yl)-[1,2,4]oxadiazole-3-ylmethoxy]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Formylfuro[3,2-c]pyridine-2-yl)-[1,2,4]oxadiazole-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-{[(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)amino]methyl}-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Ethyl(5-furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)amino]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[(5-Furo[3,2-c]pyridine-2-yl-[1,2,4]oxadiazol-3-ylmethyl)propylamino]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[(5-Furo[3,2-c]pyridine-2-yl-[1,2,4]oxadiazol-3-ylmethyl)methylamino]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethyl)methylamino]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[Ethyl(3-furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Thieno[2,3-c]pyridin-2-yl-[1,2,4]oxadiazol-3-yl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Thieno[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-yl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Thieno[2,3-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Thieno[2,3-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Thieno[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Thieno[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-yl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-[1,7]Naphthyridin-3-yl-[1,2,4]oxadiazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-[1,7]Naphthyridin-3-yl-[1,2,4]oxadiazol-3-yl)-piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-[1,7]Naphthyridin-3-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(1-Methyl-1*H*-pyrrolo[2,3-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1carboxylic acid *tert*-butyl ester; 4-[5-(1*H*-Pyrrolo[2,3-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(1*H*-Pyrrolo[2,3-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Furo[2,3-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; 4-

(5-Furo[2,3-c]pyridin-2-yl-[1,2,4]oxadiazol-3-yl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(1*H*-Pyrrolo[2,3-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-yl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(7,8-Dihydro-isoquinolin-6-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Chlorofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Chlorofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethyl)piperidine-1-carboxylic acid *tert*-butyl ester; 4-(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester; (3*S*)-3-(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethoxy)pyrrolidine-1-carboxylic acid *tert*-butyl ester; (3*R*)-3-(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethoxy)pyrrolidine-1-carboxylic acid *tert*-butyl ester; 3-(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-ylmethoxy)azetidine-1-carboxylic acid *tert*-butyl ester; 3-[2-(3-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-5-yl)-ethoxy]azetidine-1-carboxylic acid *tert*-butyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid propyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid isopropyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid ethyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid isobutyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid cyclopropylmethyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid 2-methoxycarbonyl-2-methylpropyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid (*S*)-sec-butyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid cyclobutyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid 1-methoxycarbonyl-1-methylethyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid 1-methyl-cyclobutyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid (*R*)-tetrahydrofuran-2-ylmethyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid 2-ethoxy-ethyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid 1-methyl-cyclopropyl ester; 2-[3-(1-Pyrimidin-2-ylpiperidin-4-ylmethyl)-[1,2,4]oxadiazol-5-yl]furo[3,2-c]pyridine; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid 1-carboxy-1-methylethyl ester; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidine-1-carboxylic acid 2-carboxy-2-methylpropyl ester; 4-[5-(5-Oxyfuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(5-Oxyfuro[3,2-c]pyridin-2-yl)ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(4-Cyanofuro[3,2-c]pyridin-2-ylmethoxy)-ethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[2-(4-Cyanofuro[3,2-c]pyridin-2-yl)ethyl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(7-Cyanofuro[2,3-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-

Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Cyanothieno[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid propyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid isopropyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid isobutyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid ethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid cyclobutyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid tetrahydropyran-4-yl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid (*R*)-*sec*-butyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid tetrahydrofuran-2-ylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid (*R*)-tetrahydrofuran-2-ylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid (*R*)-tetrahydrofuran-3-yl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid tetrahydrothiopyran-4-yl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 1-methoxycarbonyl-1-methylethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid methoxycarbonylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid cyclopropylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 3-ethoxy-propyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid (*S*)-*sec*-butyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 3-methyl-oxetan-3-ylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 2-ethoxy-ethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 2-methoxy-1-methylethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid tetrahydrofuran-3-ylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid (*S*)-tetrahydrofuran-3-yl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid tetrahydropyran-2-ylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 1-methyl-cyclopropyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 1-methyl-cyclobutyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 1-cyclopropylethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 1-methyl-cyclopropylmethyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 2-methyl-cyclopropylmethyl

ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 3-methoxypropyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 3-acetoxypropyl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid oxetan-3-yl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 1-oxo-hexahydro-1λ^4-thiopyran-4-yl ester; 4-[5-(4-Cyanofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid 1,1-dioxo-hexahydro-1λ^6-thiopyran-4-yl ester; 4-[5-(3-Benzyloxyfuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(3-Hydroxyfuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(4-Methylfuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-[5-(7-Iodofuro[3,2-c]pyridin-2-yl)-[1,2,4]oxadiazol-3-ylmethyl]piperidine-1-carboxylic acid *tert*-butyl ester; 4-Chloro-2-[3-(1-pyrimidin-2-ylpiperidin-4-yloxymethyl)-[1,2,4]oxadiazol-5-yl]furo[3,2-c]pyridine; 2-(3-((1-(3-Methoxypyridin-2-yl)piperidine-4-yl)methyl)-[1,2,4]-oxadiazol-5-yl)furo[3,2-c]pyridine; Ethyl 6-(4-((5-(furo[3,2-c]pyridin-2-yl)-[1,2,4]-oxadiazol-3-yl)methyl)piperidin-1-yl)nicotinate; 2-{3-[1-(4,6-Dimethyl-pyrimidin-2-yl)piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}-furo[3,2-c]pyridine; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-3'-carboxylic acid ethyl ester; 2-[4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidin-1-yl]-quinoline; 1-[4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidin-1-yl]isoquinoline; 2-[3-(1-Pyrazin-2-yl-piperidin-4-ylmethyl)-[1,2,4]oxadiazol-5-yl]-furo[3,2-c]pyridine; 2-{3-[1-(4-Methoxy-pyrimidin-2-yl)-piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}-furo[3,2-c]pyridine; [4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yl]-methanol; 2-{3-[1-(5-Ethyl-pyrimidin-2-yl)-piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}-furo[3,2-c]pyridine; 2'-Chloro-4-(5-furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl-3,4,5,6-tetrahydro-2H-[1,4']bipyridinyl; 4'-Chloro-4-(5-furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 2-[4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)piperidin-1-yl]-quinoxaline; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-6'-methyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 2-{3-[1-(6-Methyl-pyridazin-3-yl)piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}furo[3,2-c]pyridine; [4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4'-yl]-methanol; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-5'-methyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-4'-methyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 2-{3-[1-(5-Propyl-pyrimidin-2-yl)-piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}-furo[3,2-c]pyridine; 2-{3-[1-(1H-Benzoimidazol-2-yl)-piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}furo[3,2-c]pyridine; 4-(5-Furo[3,2-c]pyridin-2-yl-[1,2,4]oxadiazol-3-ylmethyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl; 2-{3-[1-(Furo[3,2-c]pyridin-4-yl)piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}-furo[3,2-c]pyridine; 2-{3-[1-(2-Chloro-pyrimidin-4-yl)piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}furo[3,2-c]pyridine; 2-{3-[1-(4-Morpholin-4-yl-pyrimidin-2-yl)-piperidin-4-

ylmethyl]-[1,2,4]oxadiazol-5-yl}-furo[3,2-c]pyridine; 2-{3-[1-(4-Trifluoromethyl-phenyl)-piperidin-4-ylmethyl]-[1,2,4]oxadiazol-5-yl}furo[3,2-c]pyridine.

Examples of GPR119 agonists are described in International Application No. PCT/GB2005/050266 (published as WO 2006/070208), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/GB2005/050266 as a GPR119 agonist is a compound of Formula (X):

$$R^1\text{-}A\text{-}V\text{-}B\text{-}R^2$$

(X)

wherein:

V is phenyl or a 6-membered heteroaryl ring containing up to three N atoms;

A is -CH=CH- or $(CH_2)_n$;

B is -CH=CH- or $(CH_2)_n$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$, C(O) or $C(O)NR^{12}$;

n is independently 0, 1, 2 or 3;

m is independently 0, 1 or 2;

R^1 is 3- or 4-pyridyl, 4- or 5-pyrimidinyl or 2-pyrazinyl, any of which may be optionally substituted by one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4}-alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, a 4- to 7-membered heterocyclyl group or a 5- or 6-membered heteroaryl group;

R^2 is 4- to 7-membered cycloalkyl substituted by R^3, $C(O)OR^3$, $C(O)R^3$ or $S(O)_2R^3$, or 4- to 7-membered heterocyclyl, containing one or two nitrogen atoms which is unsubstituted or substituted by $C(O)OR^4$, $C(O)R^3$, $S(O)_2R^3$, $C(O)NHR^4$, $P(O)(OR^{11})_2$ or a 5- or 6-membered nitrogen containing heteroaryl group;

R^3 is C_{3-8} alkyl, C_{3-8} alkenyl or C_{3-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is hydrogen, $C(O)R^7$, $S(O)_2R^8$, C_{3-7} cycloalkyl or C_{1-4} alkyl optionally substituted by OR^6, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-2} alkyl, C_{1-2} fluoroalkyl, OR^6, CN, $N(R^6)_2$ and NO_2;

R^6 are independently hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^7 is hydrogen, C_{1-4} alkyl, OR^6, $N(R^6)_2$, aryl or heteroaryl;

R^8 is C_{1-4} alkyl, C_{1-4} fluoroalkyl, aryl or heteroaryl;

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;

R^{10} is hydrogen or C_{1-4} alkyl;

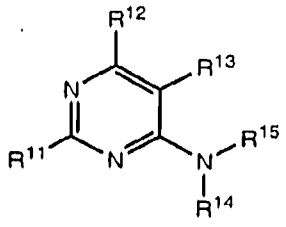
R^{11} is phenyl; and

R^{12} is hydrogen, C_{1-4} alkyl or C_{3-7} cycloalkyl.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/GB2005/050266 include the following compounds according to Formula (X) (referred to herein as **Group J1**): 4-{[Methyl-(2-pyridin-4-ylpyrimidin-4-yl)-amino]methyl}piperidine-1-carboxylic acid tert-butyl ester; 4-{[Methyl-(2-pyridin-4-ylpyrimidin-4-ylmethyl)amino]methyl}piperidine-1-carboxylic acid tert-butyl ester; 4-[([2,4']Bipyridinyl-6-ylmethylmethylamino)methyl]piperidine-1-carboxylic acid tert-butyl ester.

Examples of GPR119 agonists are described in International Application No. PCT/JP02/09350 (published as WO 03/026661), the disclosure of which is herein incorporated by reference in its entirety. Disclosed GPR119 agonist in International Application No. PCT/JP02/09350 is a compound of Formula **(XI)**:



(XI)

wherein:

$-R^{11}$ is a group represented by formula $-A^{11}-D^{11}$; wherein A^{11} is a single bond, lower alkylene, or lower alkenylene; and wherein D^{11} is an aryl, cycloalkyl, aromatic heterocycle, or a non-aromatic heterocycle, each of which may be substituted;

R^{12} is -H or a lower alkyl, which may be substituted by one or more groups selected from the group consisting of aryl, halogen, -O-lower alkyl, and -OH;

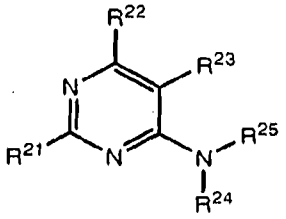
R^{13} is -H, methyl, or fluoro;

R^{14} is -H or a lower alkyl, which may be substituted by one or more halogens; and

$-R^{15}$ is a group represented by formula $-A^{15}-D^{15}$; wherein A^{15} is a single bond, lower alkylene, or lower alkenylene, each of which may be substituted; and wherein D^{15} is -H; -O-lower alkyl; an amino, which may be substituted by one or two groups selected from the group consisting of lower alkyl and aryl; or an aryl, cycloalkyl, aromatic heterocycle, or non-aromatic heterocycle, each of which may be substituted.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Examples of GPR119 agonists are described in International Application No. PCT/JP02/09350 (published as WO 03/026661), the disclosure of which is herein incorporated by reference in its entirety. Disclosed GPR119 agonist in International Application No. PCT/JP02/09350 is a compound of Formula **(XII)**:



(XII)

wherein:

R^{21} is an aryl or aromatic heterocycle, each of which may be substituted;

R^{22} is methyl or ethyl;

R^{23} is -H or fluoro;

R^{24} is -H; and

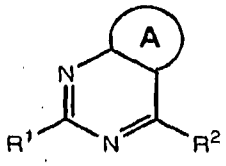
R^{25} is a lower alkyl or cycloalkyl, each of which may be substituted.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the

individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/JP02/09350 are the following compounds according to Formula (**XII**) (referred to herein as **Group L1**): 3-(2-{[2-(4-bromophenyl)-6-methylpyrimidine-4-yl]amino}ethyl)pyrrolidine 1-oxide; 2-{[2-(3-chloro-4-fluorophenyl)-6-ethylpyrimidine-4-yl]amino}ethanol; 3-(2-{[6-methyl-2-(3,4,5-trifluorophenyl)pyrmidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[2-(4-bromophenyl)-5-fluoro-6-methylpyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[2-(2,1,3-benzoxadiazol-5-yl)-6-methylpyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[6-ethyl-2-(3,4,5-trifluorophenyl)pyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 2-{[6-ethyl-2-(3,4,5-trifluorophenyl)pyrimidine-4-yl]amino}ethanol; 3-2-{[2-(2,5-difluorophenyl)-6-methylpyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[2-(2,1,3-benzoxadiazol-5-yl)-6-ethylpyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[2-(4-chloro-2-fluorophenyl)-6-methylpyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[2-(4-chloro-3-flurophenyl)-6-methylpyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[2-(5-bromo-2-flurophenyl)-6-methylpyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[6-ethyl-2-(2,3,5-trifluorophenyl)pyrimidine-4-yl]amino}ethyl)pyridine 1-oxide; 3-(2-{[6-methyl-2-(2,3,5-trifluorophenyl)pyrimidine-4-yl]amino}ethyl)pyridine 1-oxide.

Examples of GPR119 agonists are described in International Application No. PCT/JP2005/018412 (published as WO 2006/040966), the disclosure of which is herein incorporated by reference in its entirety. Disclosed GPR119 agonist in International Application No. PCT/JP2005/018412 is a compound of Formula (**XIII**):

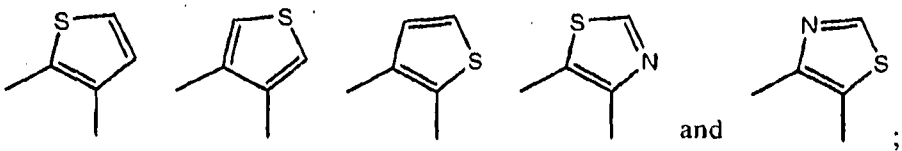


(XIII)

wherein:

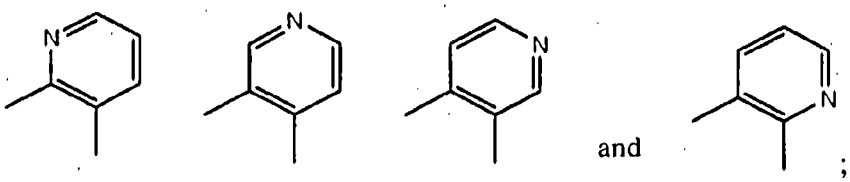
A is a ring selected from the group consisting of group X^1 and group X^2, wherein the carbon atoms comprised by this ring can be substituted by one or more groups selected from the group consisting of, lower alkyl, -O-lower alkyl, halogen, carboxyl, $-CO_2$-lower alkyl and carbamoyl;

group X^1 comprises



and ;

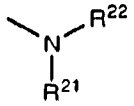
group X^2 comprises



;

-R^1 is phenyl substituted by a least one halogen; wherein this phenyl may have further substituents; and wherein when A is a ring selected from group X^2, -R^1 represents a phenyl substituted by at least three halogens;

-R^2 is a group represented by Formula (**XIIIA**)



(XIIIA)

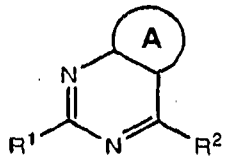
or an optionally substituted cyclic amino; wherein -R^{21} and -R^{22} are the same or different and represent -H, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, phenyl, aromatic heterocycle, non-aromatic heterocycle or -O-lower alkyl, wherein each of these groups is optionally substituted; and wherein if A is a ring selected from the group X^1, -R^2 represents an optionally substituted cyclic amino.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/JP2005/018412 are the following compounds according to Formula (**XIII**) (referred to herein as **Group M1**): 4-azepane-1-yl-2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine; 2-(4-chloro-5-fluoro-2-piperidine-1-yl phenyl)-7-methyl-4-piperidine-1-ylthieno[3,2-d]pyrimidine; [2-(4-azepane-1-ylthieno[3,2-d]pyrimidine-2-yl)-5-chloro-4-fluorophenyl]dimethylamine; 2-{5-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-2-yl}ethanol; 2-{5-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine-1-yl}ethanol; {1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperidine-3-yl} acetic acid; {1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperidine-4-ylidene}acetic acid; 2-(4-chloro-2,5-difluorophenyl)-4-piperazine-1-ylthieno[3,2-d]pyrimidine; 1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperidine-4-one; 2-{4-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperazine-1-yl}-2-oxoethanol; ethyl{4-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4yl]piperazine-1-yl}(oxo)acetate; 4-(4-acetyl-3-methylpiperazine-1-yl)-2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine; 2-{1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperidine-4-yl}acetamide; 1-[2-(4-chloro-2,5-

difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]azepane-4-ol; 1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]azepane-4-carbonitrile; (S)-3-{4-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperazine-1-yl}propane-1,2-diol; 1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]azepane-4-one oxime; 1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]azepane-4-carboxylate; ethyl({1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperidine-4-yl}oxy)acetate; (4RS,5SR)-1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4yl]azepane-4,5-diol; {4-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperazine-2-yl}methanol; 7-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]tetrahydroimidazo[1,5-a]piperazine-1,3(2H,5H)-dione; 2-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]tetrahydropyrrolo[1,2-a]piperazine-6,8(2H,7H)-dione; 4-azepane-1-yl-2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-6-carboxylate; {1-[2-(4-chloro-2,5-difluorophenyl)thieno[3,2-d]pyrimidine-4-yl]piperidine-4-yl}acetonitrile; 2-(4-chloro-2,5-difluorophenyl)-4-[4-(1H-tetrazol-5-ylmethyl)piperidine-1-yl]thieno[3,2-d]pyrimidine; 4-azepane-1-yl-2-(4-chloro-5-fluoro-2-methoxyphenyl)thieno[3,2-d]pyrimidine.

Examples of GPR119 agonists are described in International Application No. PCT/JP2005/019000 (published as WO 2006/043490), the disclosure of which is herein incorporated by reference in its entirety. Disclosed GPR119 agonist in International Application No. PCT/JP2005/019000 is a compound of Formula (**XIV**):

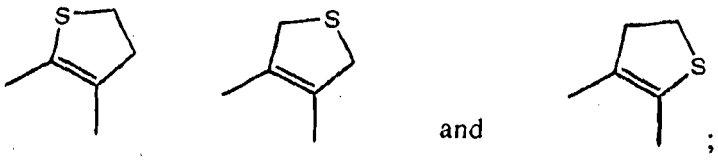


(**XIV**)

wherein:

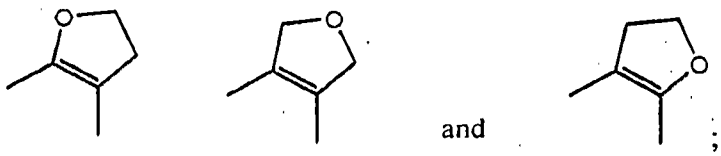
A is a ring selected from the group consisting of group X^1, group X^2, group X^3 and group X^4, wherein the carbon atoms comprised by this ring may be substituted by one or more groups selected from the group consisting of, lower alkyl, -O-lower alkyl, halogen, carboxyl, -CO_2-lower alkyl and carbamoyl, and wherein the sulfur atoms comprised by this ring may be oxidized;

group X^1 is a group comprising



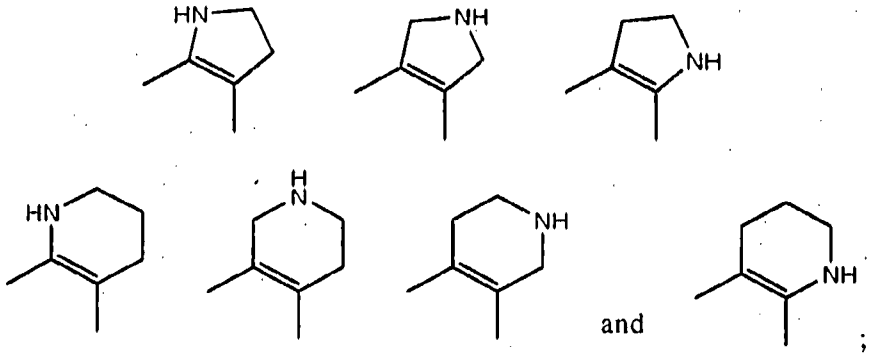
;

group X^2 is a group comprising



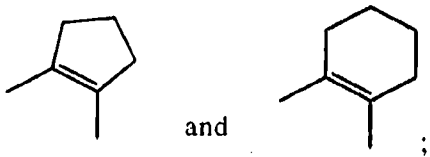
;

group X^3 is a group comprising



;

group X^4 is a group comprising



;

$-R^1$ is a group selected from (1) to (3) below:

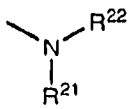
(1) Phenyl substituted by at least one halogen, wherein this phenyl may have further substituents;

(2) Cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl, each of which may be substituted;

(2) Pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, isooxazolyl, pyrazolyl, or furyl substituted by at least one halogen; wherein these rings may be substituted by one or more halogens, which are the same or different; and wherein these rings are bonded via a carbon atom comprised by these rings to position 2 of the pyrimidine ring in the Formula (**XIV**);

wherein when A is a ring selected from group X^4, $-R^1$ represents a phenyl that is substituted by at least three halogens;

$-R^2$ is the group represented by a Formula (**XIVA**)



(**XIVA**)

or an optionally substituted cyclic amino;

wherein $-R^{21}$ and $-R^{22}$ are the same or different and represent -H, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, phenyl, aromatic heterocycle, non-

aromatic heterocycle or -O-lower alkyl, wherein each of these groups may be substituted;

wherein when A is a ring selected from group X^2 or group X^3, $-R^2$ represents an optionally substituted cyclic amino.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of GPR119 agonists disclosed in International Application No. PCT/JP2005/019000 are the following compounds according to Formula (**XIV**) (referred to herein as **Group N1**): (R)-2-(4-chloro-2,5-difluorophenyl)-4-(3-methylpiperidin-1-yl)-5,7-dihydrothieno[3,4-d]pyrimidine-6,6-dioxide; 4-{1-[2-(4-chloro-2,5-difluorophenyl)-6,7-dihydro-5H-cyclopenta[d]pyrimidin-4-yl]piperidin-4-yl}butanic acid; {1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxo-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4-ylidine} acetic acid; 2-(4-chloro-2,5-difluorophenyl)-4-piperazin-1-yl-5,7-dihydrothieno[3,4-d]pyrimidine; 2-{4-[2-(4-chloro-2,5-difluorophenyl)-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperazin-1-yl}-2-oxoethanol; 2-(4-chloro-2,5-difluorophenyl)-4-[4-(methylsulfonyl)piperazin-1-yl]-5,7-dihydrothieno[3,4-d]pyrimidine; [1-(2-cyclopentyl-6,6-dioxo-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl)piperidin-4-yl]acetamide; 1-{2-[2,5-difluoro-4-(methylthio)phenyl]-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl}-1,4-diazepane-5-one; 4-[6,6-dioxide-4-(5-oxo-1,4-diazepan-1-yl)-5,7-dihydrothieno[3,4-d]pyrimidin-2-yl]-2,5-difluorobenzonitrile; 3-{1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4-yl}propane-1-ol; 2-({1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4-yl}amino)ethanol; 2-{8-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]-2,8-diazaspiro[4.5]deca-2-yl}ethanol; (2Z)-3-{1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4yl}prop-2-en-1-ol; (4R,5S)-1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]azepane-4,5-diol; N-(2-aminoethyl)-N-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]-β-alanine; {1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4-yl}acetonitrile; 1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4-yl(2-hydroxyethyl)methyl carbamate; 1-{1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4-yl}pyrrolidin-2-one; 3-{1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]piperidin-4-yl}-1,3-oxazolidin-2-one; 4-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]-N-ethylpiperazine-1-carboxamide; 2-(4-chloro-2,5-difluorophenyl)-N-cyclohexane-3-en-1-yl-5,7-dihydrothieno[3,4-d]pyrimidine-4-amine 6,6-dioxide; 3-{1-[2-(4-chloro-2,5-difluorophenyl)-6,6-dioxide-5,7-dihydrothieno[3,4-d]pyrimidin-4-yl]-4-hydroxypiperidin-4-yl}propyl acetate.

Examples of GPR119 agonists are described in International Application No. PCT/GB2006/050176 (published as WO 2007/003960), the disclosure of which is herein incorporated by reference in its entirety.

Examples of GPR119 agonists are described in International Application No. PCT/GB2006/050177 (published as WO 2007/003961), the disclosure of which is herein incorporated by reference in its entirety.

Examples of GPR119 agonists are described in International Application No. PCT/GB2006/050178 (published as WO 2007/003962), the disclosure of which is herein incorporated by reference in its entirety.

Examples of GPR119 agonists are described in International Application No. PCT/GB2006/050182 (published as WO 2007/003964), the disclosure of which is herein incorporated by reference in its entirety.

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**I**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**II**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**III**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**IV**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**V**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**VI**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**VI**), provided that the compound is not identical to 4-(5-piperidin-4-yl-[1,2,4]oxadiazol-3-yl)pyridine, 4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid butyl ester, 4-[5-(4-butylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine, 3-[5-(4-butylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine, or 3-[5-(4-propylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine.

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**VII**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**VIII**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**IX**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**X**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**XI**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**XII**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**XII**), provided that when in Formula (**XII**) R^{22} is methyl and R^{23} is -H, R^{25} in Formula (**XII**) is not: an unsubstituted lower alkyl; ethyl or propyl, each of which is substituted by a dimethylamino or a diisopropylamino; methyl substituted by a carbamoyl, which is substituted by two identical or different groups selected from the group consisting of lower alkyl and phenyl; or methyl substituted by phenyl, which may be substituted.

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**XII**), provided that the compound is not identical to 6-methyl-N-(2-morpholine-4-ylethyl)-2-

phenylpyrimidine-4-amine, 6-methyl-2-(4-methoxyphenyl)-N-(2-morpholine-4-ylethyl)pyrimidine-4-amine, 2-{[6-methyl-2-(6-methylpyridine-2-yl)pyrimidine-4-yl]amino}ethanol, 2-{[2-(4-bromophenyl)-6-methylpyrimidine-4-yl]amino}ethanol, or [2-(4-bromophenyl)-6-methylpyrimidine-4-yl](cyclohexyl)amino.

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**XIII**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**XIV**).

In one aspect of the present invention, the GPR119 agonist is a compound of Formula (**XIV**), provided that the compound is not identical to 2-(2-fluorophenyl)-N,N-dimethyl-5,7-dihydrothieno[3,4-d]pyrimidine-4-amine or 2-cyclopropyl-4-piperazin-1-yl-5,7-dihydrothieno[3,4-d]pyrimidine.

In one aspect of the present invention, the GPR119 agonist is a compound selected from Group A1, Group B1, Group B2, Group B3, Group B4, Group B5, Group C1, Group C2, Group C3, Group C4, Group C5, Group C6, Group C7, Group C8, Group C9, Group C10, Group D1, Group D2, Group D3, Group D4, Group D5, Group D6, Group D7, Group D8, Group D9, Group D10, Group D11, Group D12, Group D13, Group D14, Group E1, Group E2, Group F1, Group G1, Group G2, Group G3, Group H1, Group I1, Group J1, Group L1, Group M1, or Group N1.

In one aspect, the GPR119 agonist is selected from the left column of Table D. It is expressly contemplated that each individual GPR119 agonist from the left column of Table D is a separate embodiment within the scope of the present invention.

In one aspect, the GPR119 agonist is selected from any set of compounds selected from the left column of Table D.

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/US2004/001267 (published as WO 04/065380).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/US2004/005555 (published as WO 04/076413).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/US2004/022327 (published as WO 05/007647).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/US2004/022417 (published as WO 05/007658).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/US2005/019318 (published as WO 2005/121121).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2004/050046 (published as WO 2005/061489).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/US06/00567 (published as WO 2006/083491).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2005/050264 (published as WO 2006/067531).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2005/050265 (published as WO 2006/067532).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2005/050266 (published as WO 2006/070208).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/JP02/09350 (published as WO 03/026661).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/JP2005/018412 (published as WO 06/040966).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/JP2005/019000 (published as WO 2006/043490).

In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2006/050176 (published as WO 2007/003960).

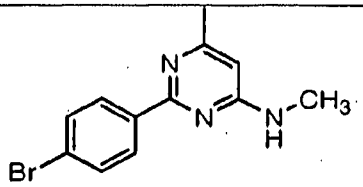
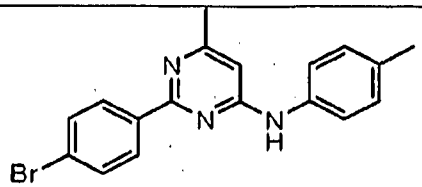
In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2006/050177 (published as WO 2007/003961).

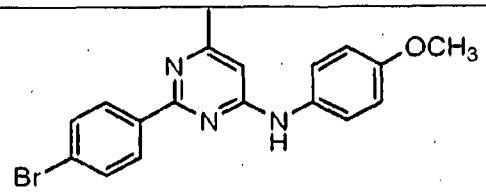
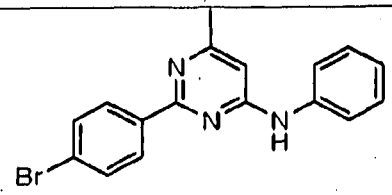
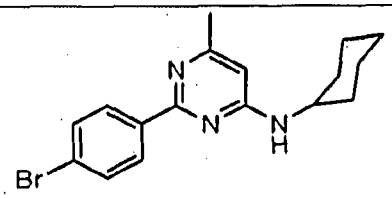
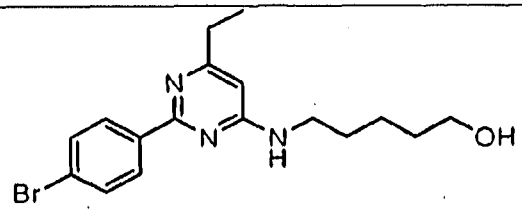
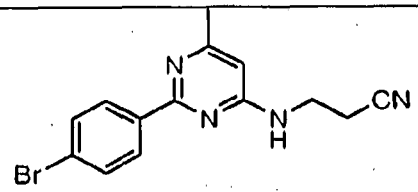
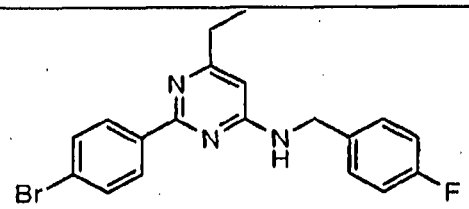
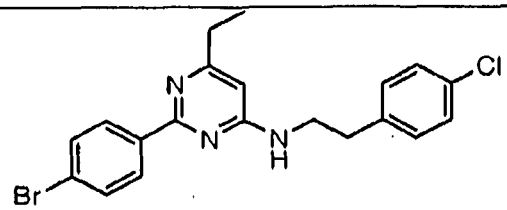
In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2006/050178 (published as WO 2007/003962).

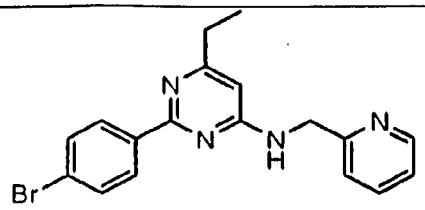
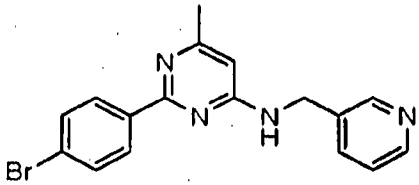
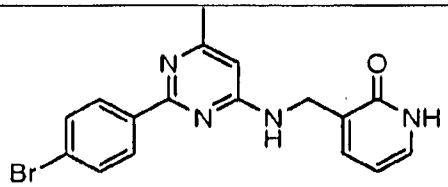
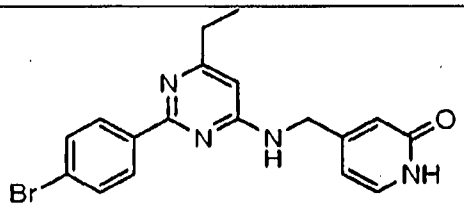
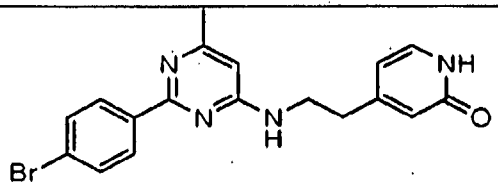
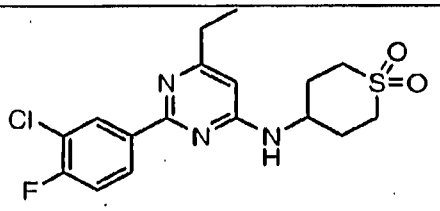
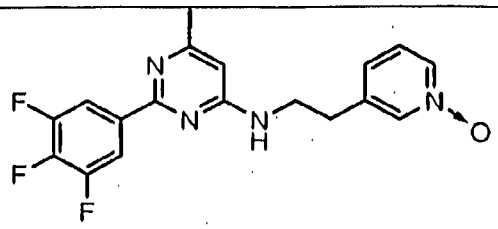
In one aspect, the GPR119 agonist is identical to a compound disclosed in International Application No. PCT/GB2006/050182 (published as WO 2007/003964).

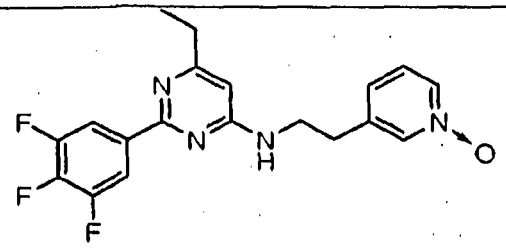
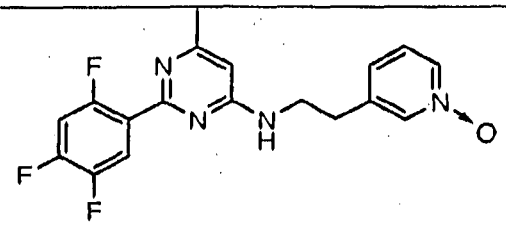
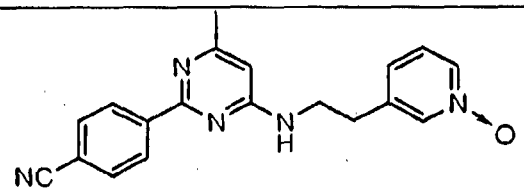
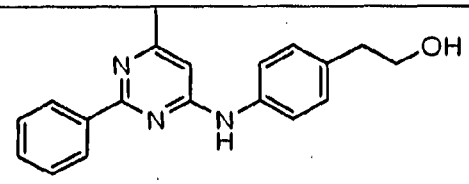
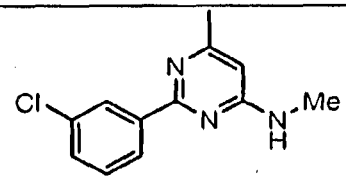
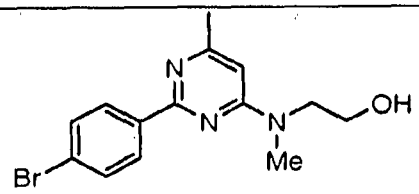
Other examples of GPR119 agonists may be found in International Application No. PCT/JP02/09350 (published as WO 03/026661), the disclosure of which is herein incorporated by reference in its entirety. GPR119 agonists disclosed in International Application No. PCT/JP02/09350 include but are not limited to the compounds in Table A.

TABLE A

Cmpd No.	Chemical Structure	Chemical Name
1A		[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-methyl-amine
2A		[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-p-tolyl-amine

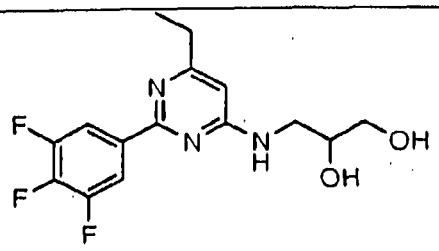
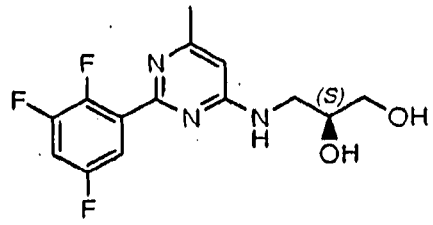
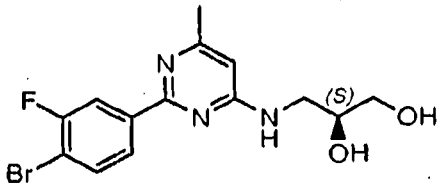
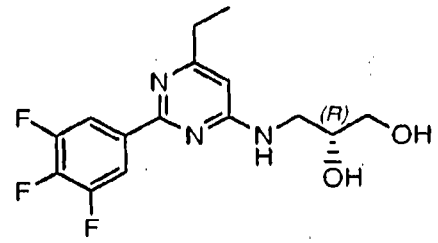
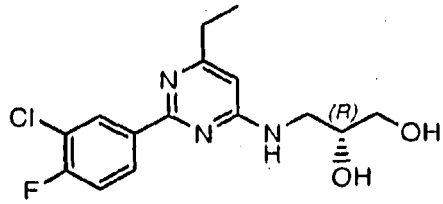
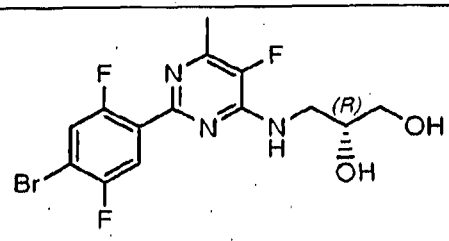
Cmpd No.	Chemical Structure	Chemical Name
3A		[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-(4-methoxy-phenyl)-amine
4A		[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-phenyl-amine
5A		[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-cyclohexyl-amine
6A		5-[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-ylamino]-pentan-1-ol
7A		3-[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-ylamino]-propionitrile
8A		[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-yl]-(4-fluoro-benzyl)-amine
9A		[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-yl]-[2-(4-chloro-phenyl)-ethyl]-amine

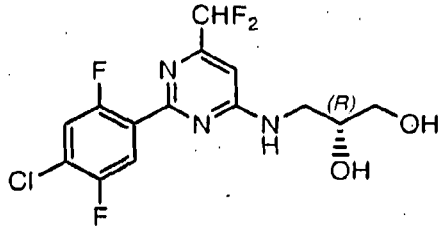
Cmpd No.	Chemical Structure	Chemical Name
10A		[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-yl]-pyridin-2-ylmethyl-amine
11A		[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-pyridin-3-ylmethyl-amine
12A		3-{[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-ylamino]-methyl}-1H-pyridin-2-one
13A		4-{[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-ylamino]-methyl}-1H-pyridin-2-one
14A		4-{2-[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one
15A		[2-(3-Chloro-4-fluoro-phenyl)-6-ethyl-pyrimidin-4-yl]-(1,1-dioxo-hexahydro-1l6-thiopyran-4-yl)-amine
16A		[6-Methyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-yl]-[2-(1-oxy-pyridin-3-yl)-ethyl]-amine

Cmpd No.	Chemical Structure	Chemical Name
17A		[6-Ethyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-yl]-[2-(1-oxy-pyridin-3-yl)-ethyl]-amine
18A		[6-Methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-yl]-[2-(1-oxy-pyridin-3-yl)-ethyl]-amine
19A		4-{4-Methyl-6-[2-(1-oxy-pyridin-3-yl)-ethylamino]-pyrimidin-2-yl}-benzonitrile
20A		2-[4-(6-Methyl-2-phenyl-pyrimidin-4-ylamino)-phenyl]-ethanol
21A		[2-(3-Chloro-phenyl)-6-methyl-pyrimidin-4-yl]-methyl-amine
22A		2-{[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-methyl-amino}-ethanol; compound with methane

Examples of GPR119 agonists may be found in International Application JP 2004269468, the disclosure of which is herein incorporated by reference in its entirety. GPR119 agonists disclosed in JP 2004269468 include but are not limited to the compounds in Table B.

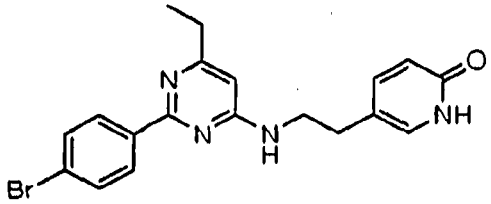
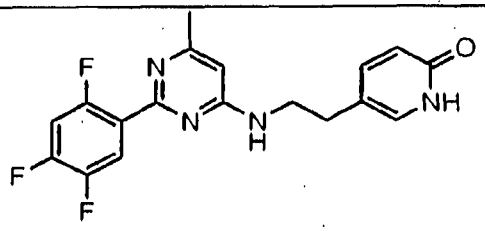
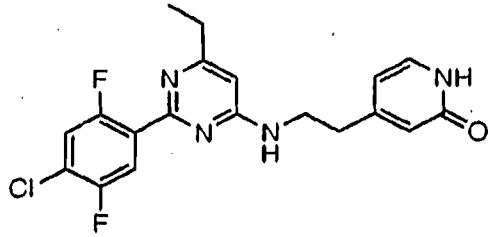
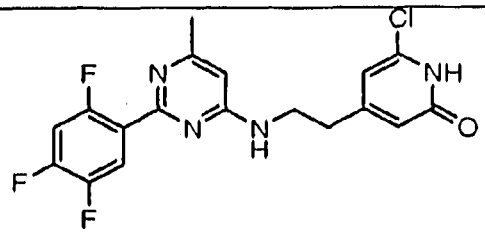
TABLE B

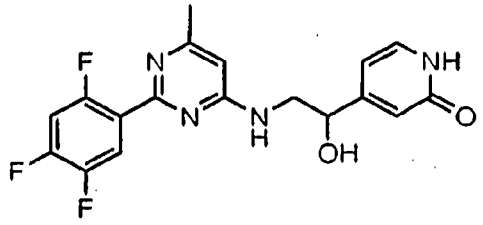
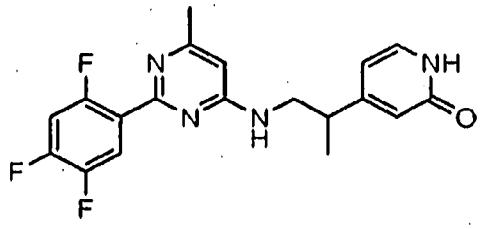
Cmpd No.	Chemical Structure	Chemical Name
1B		3-[6-Ethyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-propane-1,2-diol
2B		(*S*)-3-[6-Methyl-2-(2,3,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-propane-1,2-diol
3B		(*S*)-3-[2-(4-Bromo-3-fluoro-phenyl)-6-methyl-pyrimidin-4-ylamino]-propane-1,2-diol
4B		(*R*)-3-[6-Ethyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-propane-1,2-diol
5B		(*R*)-3-[2-(3-Chloro-4-fluoro-phenyl)-6-ethyl-pyrimidin-4-ylamino]-propane-1,2-diol
6B		(*R*)-3-[2-(4-Bromo-2,5-difluoro-phenyl)-5-fluoro-6-methyl-pyrimidin-4-ylamino]-propane-1,2-diol

Cmpd No.	Chemical Structure	Chemical Name
7B		(*R*)-3-[2-(4-Chloro-2,5-difluoro-phenyl)-6-difluoromethyl-pyrimidin-4-ylamino]-propane-1,2-diol

Examples of GPR119 agonists may be found in International Application JP 2004269469, the disclosure of which is herein incorporated by reference in its entirety. GPR119 agonists disclosed in JP 2004269469 include but are not limited to the compounds in Table C.

TABLE C

Cmpd No.	Chemical Structure	Chemical Name
1C		5-{2-[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one
2C		5-{2-[6-Methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one
3C		4-{2-[2-(4-Chloro-2,5-difluoro-phenyl)-6-ethyl-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one
4C		6-Chloro-4-{2-[6-methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one

Cmpd No.	Chemical Structure	Chemical Name
5C		4-{1-Hydroxy-2-[6-methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one
6C		4-{1-Methyl-2-[6-methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one

In one aspect, the GPR119 agonist is identical to a compound disclosed in WO 03/026661.

In one aspect, the GPR119 agonist is a compound selected from Table A.

In one aspect, the GPR119 agonist is identical to a compound disclosed in JP 2004269468.

In one aspect, the GPR119 agonist is a compound selected from Table B.

In one aspect, the GPR119 agonist is identical to a compound disclosed in JP 2004269469.

In one aspect, the GPR119 agonist is a compound selected from Table C.

In one aspect of the present invention, the GPR119 agonist has an EC_{50} of less than about 10 μM, less than about 1 μM, less than about 100 nM, less than about 75 nM, less than about 50 nM, less than about 25 nM, less than about 20 nM, less than about 15 nM, less than about 10 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, or less than about 1 nM. In certain embodiments, the GPR119 agonist has an EC_{50} of less than about 50 nM, less than about 25 nM, less than about 20 nM, less than about 15 nM, less than about 10 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, or less than about 1 nM.

In one aspect of the present invention, the GPR119 agonist is a selective GPR119 agonist, wherein the selective GPR119 agonist has a selectivity for GPR119 over corticotrophin-releasing factor-1 (CRF-1) receptor of at least about 10-fold, of at least about 100-fold, or of at least about 1000-fold. In one aspect of the present invention, the GPR119 agonist is a selective GPR119 agonist, wherein the selective GPR119 agonist has a selectivity for GPR119 over corticotrophin-releasing factor-1 (CRF-1) receptor of at least about 100-fold.

In one aspect of the present invention, the GPR119 agonist is a small molecule.

In one aspect of the present invention, the GPR119 agonist is orally active.

It is expressly contemplated that a GPR119 agonist of the invention is an agonist of an endogenous GPR119.

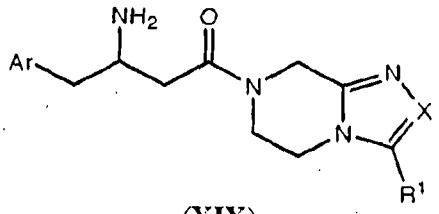
In one aspect of the present invention, the GPR119 agonist is an agonist of human GPR119 (*e.g.*, human GPR119, GenBank® Accession No. AAP72125 and alleles thereof).

In one aspect of the present invention, any one or more GPR119 agonist can be excluded from any embodiment of the present invention.

DPP-IV Inhibitors

The class of DPP-IV inhibitors useful in the novel therapeutic combinations of the present invention include compounds which exhibit an acceptably high affinity for DPP-IV. The DPP-IV inhibitor or pharmaceutically acceptable salt may be any DPP-IV inhibitor, and in particular embodiment a selective dipeptidyl peptidase inhibitor, and in further particular embodiment a selective DPP-IV inhibitor.

Examples of DPP-IV inhibitors are described in International Application No. PCT/US02/21349 (published as WO 03/004498), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US02/21349 as a DPP-IV inhibitor is a compound of Formula (**XIX**):



(XIX)

wherein:

Ar is phenyl which is unsubstituted or substituted with 1-5 of R^3, wherein R^3 is independently selected from the group consisting of:

(1) halogen,

(2) $C_{1\text{-}6}$alkyl, which is linear or branched and is unsubstituted or substituted with 1-5 halogens,

(3) $OC_{1\text{-}6}$alkyl, which is linear or branched and is unsubstituted or substituted with 1-5 halogens, and

(4) CN;

X is selected from the group consisting of:

(1) N, and

(2) CR^2;

R^1 and R^2 are independently selected from the group consisting of:

(1) hydrogen,

(2) CN,

(3) $C_{1\text{-}10}$alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or

substituted with 1-5 substituents independently selected from halogen, CN, OH, R^4, OR^4, $NHSO_2R^4$, SO_2R^4, CO_2H, and CO_2C_{1-6}alkyl, wherein the CO_2C_{1-6}alkyl is linear or branched,

(4) phenyl which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH, R^4, OR^4, $NHSO_2R^4$, SO_2R^4, CO_2H, and CO_2C_{1-6}alkyl, wherein the CO_2C_{1-6}alkyl is linear or branched, and

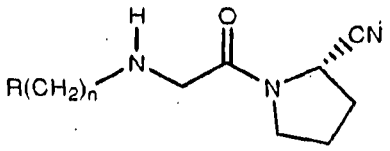
(5) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen, C_{1-6}alkyl, and OC_{1-6}alkyl, wherein the C_{1-6}alkyl and OC_{1-6}alkyl are linear or branched and optionally substituted with 1-5 halogens;

R^4 is C_{1-6}alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen, CO_2H, and CO_2C_{1-6}alkyl, wherein the CO_2C_{1-6}alkyl is linear or branched.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of DPP-IV inhibitors disclosed in International Application No. PCT/US02/21349 include the following compounds according to Formula **(XIX)** (referred to herein as **Group S1**): 7-[(3*R*)-3-Amino-4-(3,4-difluorophenyl)butanoyl]-2-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine; 7-[(3*R*)-3-Amino-4-(2,5-difluorophenyl)butanoyl]-2-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine; 7-[(3*R*)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-2-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine; 7-[3(*R*)-3-Amino-4-(3,4-difluorophenyl(butanoyl]-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine; 7-[(3*R*)-3-Amino-4-(3,4-difluorophenyl)butanoyl]-3-ethyl-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-*a*]pyrazine; 7-[(3*R*)-3-Amino-4-(2,5-difluorophenyl)butanoyl]-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-*a*]pyrazine; 7-[(3*R*)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-*a*]pyrazine.

Examples of DPP-IV inhibitors are described in International Application No. PCT/EP99/09708 (published as WO 00/34241), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/EP99/09708 as a DPP-IV inhibitor is a compound of Formula **(XX)**:



(XX)

wherein:

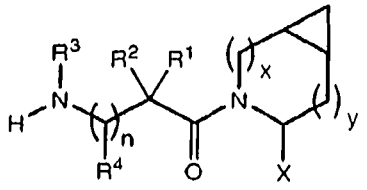
R is substituted adamantyl; and

n is 0 to 3.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of DPP-IV inhibitors disclosed in International Application No. PCT/EP99/09708 include the following compounds according to Formula (**XX**) (referred to herein as **Group T1**): pyrrolidine, 1-[[(3,5-dimethyl-1-adamantyl)amino]-acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[(3-ethyl-1-adamantyl)amino]acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[(3-methoxy-1-adamantyl)amino]-acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[[3-[[(t-butylamino)carbonyl]oxy]-1-adamantyl]amino]acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[[3-[[[(4-methoxyphenyl)amino]carbonyl]oxy]-1-adamantyl]amino]acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[[3-[[(phenylamino)carbonyl]oxy]-1-adamantyl]amino]acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[(5-hydroxy-2-adamantyl)amino]-acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[(3-acetyloxy-1-adamantyl)amino]-acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[[3-[[[(diisopropyl)amino]carbonyl]oxy]-1-adamantyl]amino]acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[[3-[[[(cyclohexyl)amino]carbonyl]oxy]-1-adamantyl]amino]acetyl]-2-cyano-, (S)-; pyrrolidine, 1-[[(3-ethoxy-1-adamantyl)amino]acetyl]-2-cyano-, (S)-.

Examples of DPP-IV inhibitors are described in International Application No. PCT/US01/07151 (published as WO 01/68603), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US01/07151 as a DPP-IV inhibitor is a compound of Formula (**XXI**):



(XXI)

wherein:

x is 0 or 1 and y is 0 or 1, provided that

x = 1 when y = 0 and

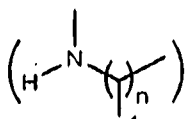
x = 0 when y = 1;

n is 0 or 1;

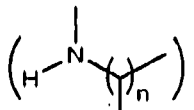
X is H or CN;

R^1, R^2, R^3 and R^4 are the same or different and are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, hydroxytricycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxycarbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, arylamino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro, cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxycarbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxycarbonylamino, alkylsulfonyl, aminosulfinyl, aminosulfonyl, alkylsulfinyl, sulfonamido or sulfonyl;

and R^1 and R^3 may optionally be taken together to form $-(CR^5R^6)_m-$ where m is 2 to 6, and R^5 and R^6 are the same or different and are indpependently selected from hydroxy, alkoxy, H, alkyl, alkenyl, alkynyl, cycloalkyl, halo, amino, substituted amino, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or R^1 and R^4 may optionally be taken together to form $-(CR^7R^8)_p-$ wherein p is 2 to 6, and R^7 and R^8 are the same or different and are independently selected from hydroxy, alkoxy, cyano, H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halo, amino, substituted amino, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, alkoxycarbonyl, aryloxycarbonyl, or alkylaminocarbonylamino, or optionally R^1 and R^3 together with



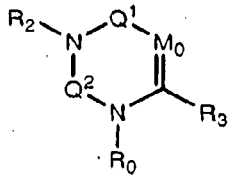
R^4 form a 5 to 7 membered ring containing a total of 2 to 4 heteroatoms selected from N, O, S, SO, or SO_2;



or optionally R^1 and R^3 together with R^4 form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Examples of DPP-IV inhibitors are described in International Application No. PCT/US2004/042209 (published as WO 2005/095381), the disclosure of which is herein incorporated by reference in its entirety. Disclosed in International Application No. PCT/US2004/042209 as a DPP-IV inhibitor is a compound of Formula (**XXII**):



(**XXII**)

wherein:

M_0 is –C–LX, N or CR_4;

Q^1 and Q^2 are each independently selected from the group consisting of CO, CS, SO, SO_2, and C=NR_9;

R_0 is R_1 or –LX, with the proviso that only one of R_0 and M_0 is –LX;

R_1 is hydrogen or is selected from the group consisting of halo, perhalo(C_{1-10})alkyl, amino, cyano, thio, (C_{1-10})alkyl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, aryl, heteroaryl, carbonyl (C_{1-3})alkyl, thiocarbonyl (C_{1-3})alkyl, sulfonyl (C_{1-3})alkyl, sulfinyl C($_{1-3}$)alkyl, imino (C_{1-3})alkyl, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl group, imino group, sulfonyl group and sulfinyl group, each substituted or unsubstituted;

R_2 is hydrogen or selected from the group consisting of (C_{1-10})alkyl, C($_{3-12}$)cycloalkyl, (C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl(C_{1-5})alkyl, hetero(C_{3-12})cycloalkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl, hetero(C_{4-12})bicycloaryl, hetero(C_{4-12})bicycloaryl(C_{1-5})alkyl, carbonyl (C_{1-3})alkyl, thiocarbonyl (C_{1-3})alkyl, sulfonyl (C_{1-3})alkyl, sulfinyl (C_{1-3})alkyl, imino (C_{1-3})alkyl, amino, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl group, imino group, sulfonyl group and sulfinyl group, each substituted or unsubstituted;

R_3 is selected from the group consisting of perhalo(C_{1-10})alkyl, amino, (C_{1-10})alkyl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, aryl, heteroaryl, carbonyl (C_{1-3})alkyl, thiocarbonyl (C_{1-3})alkyl, sulfonyl (C_{1-3})alkyl, sulfinyl (C_{1-3})alkyl, imino (C_{1-3})alkyl, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl group, imino group, sulfonyl group and sulfinyl group, each substituted or unsubstituted, and a substituted or unsubstituted 3, 4, 5, 6 or 7 membered ring;

R_4 is hydrogen or is selected from the group consisting of halo, perhalo(C_{1-10})alkyl, amino, cyano, thio, (C_{1-10})alkyl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, aryl, heteroaryl, carbonyl (C_{1-3})alkyl, thiocarbonyl (C_{1-3})alkyl, sulfonyl (C_{1-3})alkyl, sulfinyl (C_{1-3})alkyl, imino (C_{1-3})alkyl, hydroxy, alkoxy, aryloxy, heteroaryloxy, carbonyl group, imino group, sulfonyl group and sulfinyl group, each substituted or unsubstituted;

R_9 is hydrogen or is selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, bicycloaryl, and heterobicycloaryl, each substituted or unsubstituted;

L is a linker providing 1, 2 or 3 atom separation between X and the ring to which L is attached, wherein the atoms of the linker providing the separation are selected from the group consisting of carbon, oxygen, nitrogen, and sulfur; and

X is selected from the group consisting of (C_{1-10})alkyl, (C_{3-12})cycloalkyl, hetero(C_{3-12})cycloalkyl, aryl(C_{1-10})alkyl, heteroaryl(C_{1-5})alkyl, (C_{9-12})bicycloaryl, hetero(C_{4-12})bicycloaryl, carbonyl (C_{1-3})alkyl, thiocarbonyl (C_{1-3})alkyl, sulfonyl (C_{1-3})alkyl, sulfinyl (C_{1-3})alkyl, imino (C_{1-3})alkyl, amino, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, heteroaryloxy, alkenyl, alkynyl, carbonyl group, cyano, imino group, sulfonyl group and sulfinyl group, each substituted or unsubstituted.

The present invention also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds of the invention. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

Specific examples of DPP-IV inhibitors disclosed in International Application No. PCT/US2004/042209 include the following compounds according to Formula **(XXII)** (referred to herein as **Group V1**): 2-(6-Chloro-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl)-benzonitrile; 2-(6-Chloro-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl)-benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-3-ethyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3-Amino-piperidin-1yl]-5-chloro-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 6-[3-Amino-piperidin-1-yl]-1-(2-bromo-benzyl)-1H-pyrimidine-2,4-dione; 6-[3-Amino-

piperidin-1-yl]-1-(2-iodo-benzyl)-1H-pyrimidine-2,4-dione; 6-[3-Amino-piperidin-1-yl]-1-(2-bromo-5-fluoro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 6-[3-Amino-piperidin-1-yl]-1-(2-chloro-5-fluoro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 6-[3-Amino-piperidin-1-yl]-1-(2-chloro-4-fluoro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 6-[3-Amino-piperidin-1-yl]-1-(2-bromo-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 2-{6-[Azepan-3(±)-ylamino]-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3(±)-Amino-azepan-1-yl]-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-[6-(2-Amino-ethylamino)-3-ethyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl]-benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-3-(3-cyano-benzyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-3-(4-cyano-benzyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}benzonitrile; 2-[6-(3-Amino-piperidin-1-yl)-3-(1H-benzoimidazol-2-ylmethyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl]-benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-2,4-dioxo-3-(4-pyrazol-1-yl-benzyl)-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3-Amino-piperidin-1-yl]-2,4-dioxo-3-(3-pyrrol-1-yl-benzyl)-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 6-[3-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,6-dioxo-3,6-dihydro-2H-pyrimidin-1-ylmethyl]-thiophene-3-carbonitrile; 3-{4-[3-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,6-dioxo-3,6-dihydro-2H-pyrimidin-1-ylmethyl}-benzoic acid methyl ester; 3-{4-[3-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,6-dioxo-3,6-dihydro-2H-pyrimidin-1-ylmethyl}-benzoic acid; 6-[3-Amino-piperidin-1-yl]-1,3-bis-(2-bromo-5-fluoro-benzyl)-1H-pyrimidine-2,4-dione; 2-{6-[3(R)-Amino-piperidin-1-yl]-5-chloro-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 6-[3(R)-Amino-piperidin-1-yl]-1-(2,5-*di*-chloro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 6-[3(R)-Amino-piperidin-1-yl]-1-(2-chloro-3,6-*di*-fluoro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; (R)-2-((6-(3-amino-3-methylpiperidin-1-yl)-3-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl)-4-fluorobenzonitrile; 2-[6-(3-Amino-piperidin-1-yl)-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl]-4-fluoro-benzonitrile.

Specific examples of DPP-IV inhibitors disclosed in International Application No. PCT/US2004/042209 include the following compounds according to Formula (**XXII**) (referred to herein as **Group V2**): 2-{6-[3(R)-Amino-piperidin-1-yl]-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}benzonitrile; 2-{6-[3(R)-Amino-piperidin-1-yl]-3-ethyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3(R)-Amino-piperidin-1-yl]-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3(R)-Amino-piperidin-1-yl]-5-chloro-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 6-[3(R)-Amino-piperidin-1-yl]-1-(2-bromo-benzyl)-1H-pyrimidine-2,4-dione; 6-[3(R)-Amino-piperidin-1-yl]-1-(2-iodo-benzyl)-1H-pyrimidine-2,4-dione; 6-[3(R)-Amino-piperidin-1-yl]-1-(2-bromo-5-fluoro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 6-{[3(R)-Amino-piperidin-1-yl]-1-(2-chloro-5-fluoro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 6-[3(R)-Amino-piperidin-1-yl]-1-(2-chloro-4-fluoro-benzyl)-3-methyl-1H-pyrimidine-2,4-dione; 6-[3(R)-Amino-piperidin-1-yl]-1-(2-bromo-benzyl)-3-methyl-1H-pyrimidine-

2,4-dione; 2-{6-[3(R)-Amino-piperidin-1-yl]-3-(3-cyano-benzyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3(R)-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3(R)-Amino-piperidin-1-yl]-3-(4-cyano-benzyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1ylmethyl}-benzonitrile; 2-[6-(3-Amino-piperidin-1-yl)-3-(1H-benzoimidazol-2-ylmethyl)-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl]-benzonitrile; 2-{6-[3(R)-Amino-piperidin-1-yl]-2,4-dioxo-3-(4-pyrazol-1-yl-benzyl)-3,4-dihydro-2H-pyrimidin-1-ylmethyl}-benzonitrile; 2-{6-[3(R)-Amino-piperidin-1-yl]-2,4-dioxo-3-(3-pyrrol-1-yl-benzyl)-3,4-dihydro-2H-pyrimidin-1-ylmethyl)-benzonitrile; 6-[3(R)-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,6-dioxo-3,6-dihydro-2H-pyrimidin-1-ylmethyl]-thiophene-3-carbonitrile; 3-{4-[3(R)-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,6-dioxo-3,6-dihydro-2H-pyrimidin-1-ylmethyl}-benzoic acid methyl ester; 3-{4-[3(R)-Amino-piperidin-1-yl]-3-(2-cyano-benzyl)-2,6-dioxo-3,6-dihydro-2H-pyrimidin-1-ylmethyl}-benzoic acid; 6-[3(R)-Amino-piperidin-1-yl]-1,3-bis-(2-bromo-5-fluoro-benzyl)-1H-pyrimidine-2,4-dione; 2-[6-(3(R)-Amino-piperidin-1-yl)-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl]-4-fluoro-benzonitrile.

Examples of DPP-IV inhibitors are described in Villhauer et al., J Med Chem (2003) 46:2774-2789, for LAF237; Ahren et al, J Clin Endocrinol Metab (2004) 89:2078-2084; Villhauer et al., J Med Chem (2002) 45:2362-2365 for NVP-DPP728; Ahren et al, Diabetes Care (2002) 25:869-875 for NVP-DPP728; Peters et al., Bioorg Med Chem Lett (2004) 14:1491-1493; Caldwell et al., Bioorg Med Chem Lett (2004) 14:1265-1268; Edmondson et al., Bioorg Med Chem Lett (2004) 14:5151-5155; and Abe et al., J Nat Prod (2004) 67:999-1004; the disclosure of each of which is herein incorporated by reference in its entirety.

Specific examples of DPP-IV inhibitors include, but are not limited to, dipeptide derivatives or dipeptide mimetics such as alanine-pyrrolidide, isoleucine-thiazolidide, and the pseudosubstrate N-valyl prolyl, O-benzoyl hydroxylamine, as described e.g. in U.S. Pat. No. 6,303,661, the disclosure of which is herein incorporated by reference in its entirety.

Examples of DPP-IV inhibitors may be found in U.S. Pat. Nos. 7,074,794, 7,060,722, 7,053,055, 7,026,316, 7,022,718, 6,949,515, 6,897,222, 6,869,947, 6,867,205, 6,861,440, 6,849,622, 6,812,350, 6,803,357, 6,800,650, 6,727,261, 6,716,843, 6,710,040, 6,706,742, 6,645,995, 6,617,340, 6,699,871, 6,573,287, 6,432,969, 6,395,767, 6,380,398, 6,303,661, 6,242,422, 6,166,063, 6,100,234, 6,040,145, the disclosure of each of which is herein incorporated by reference in its entirety. Examples of DPP-IV inhibitors may be found in U.S. Pat. Appl. Nos. 2006142576, 2006135767, 2006135512, 2006111336, 2006074087, 2006069116, 2006052382, 2006046978, 2006040963, 2006039974, 2006024313, 2006014764, 2005059724, 2005059716, 2005043292, 2005038020, 2005032804, 2005004205, 2004259903, 2004259902, 2004259883, 2004254226, 2004242898, 2004229926, 2004180925, 2004176406, 2004138214, 2004116328, 2004110817, 2004106656, 2004097510, 2004087587, 2004082570, 2004077645, 2004072892, 2004063935, 2004034014, 2003232788, 2003225102, 2003216450, 2003216382, 2003199528, 2003195188, 2003162820,

2003149071, 2003134802, 2003130281, 2003130199, 2003125304, 2003119750, 2003119738, 2003105077, 2003100563, 2003087950, 2003078247, 2002198205, 2002183367, 2002103384, 2002049164, 2002006899, the disclosure of each of which is herein incorporated by reference in its entirety.

Examples of DPP-IV inhibitors may be found in International Applications WO 2006/071762, wo 2006/071752, WO 2006/068978, WO 2006/068163, WO 2006/058628, WO 2006/058064, WO 2006/040625, WO 2006/039325, WO 2006/033848, WO 2006/030847, WO 2006/027204, WO 2006/023750, WO 2006/020017, WO 2006/015699, WO 2006/015691, WO 2006/013104, WO 2006/012441, WO 2006/012395, WO 2006/011035, WO 2006/009886, WO 2005/123685, WO 2005/121131, WO 2005/121089, WO 2005/120494, WO 2005/118555, WO 2005/116029, WO 2005/116014, WO 2005/115982, WO 2005/108382, WO 2005/106011, WO 2005/100334, WO 2005/095339, WO 2005/094323, WO 2005/087235, WO 2005/082849, WO 2005/082348, WO 2005/079795, WO 2005/075426, WO 2005/072530, WO 2005/063750, WO 2005/058849, WO 2005/049022, WO 2005/047297, WO 2005/044195, WO 2005/042533, WO 2005/042488, WO 2005/040095, WO 2005/037828, WO 2005/037779, WO 2005/034940, WO 2005/033099, WO 2005/032590, WO 2005/030751, WO 2005/030127, WO 2005/026148, WO 2005/025554, WO 2005/023762, WO 2005/020920, WO 05/19168, WO 05/12312, WO 05/12308, WO 05/12249, WO 05/11581, WO 05/09956, WO 05/03135, WO 05/00848, WO 05/00846, WO 04/112701, WO 04/111051, WO 04/111041, WO 04/110436, WO 04/110375, WO 04/108730, WO 04/104216, WO 04/104215, WO 04/103993, WO 04/103276, WO 04/99134, WO 04/96806, WO 04/92128, WO 04/87650, WO 04/87053, WO 04/85661, WO 04/85378, WO 04/76434, WO 04/76433, WO 04/71454, WO 04/69162, WO 04/67509, WO 04/64778, WO 04/58266, WO 04/52362, WO 04/52850, WO 04/50022, WO 04/50658, WO 04/48379, WO 04/46106, WO 04/43940, WO 04/41820, WO 04/41795, WO 04/37169, WO 04/37181, WO 04/33455, WO 04/32836, WO 04/20407, WO 04/18469, WO 04/18468, WO 04/18467, WO 04/14860, WO 04/09544, WO 04/07468, WO 04/07446, WO 04/04661, WO 04/00327, WO 03/106456, WO 03/104229, WO 03/101958, WO 03/101448, WO 03/99279, WO 03/95425, WO 03/84940, WO 03/82817, WO 03/80633, WO 03/74500, WO 03/72556, WO 03/72528, WO 03/68757, WO 03/68748, WO 03/57666, WO 03/57144, WO 03/55881, WO 03/45228, WO 03/40174, WO 03/38123, WO 03/37327, WO 03/35067, WO 03/35057, WO 03/24965, WO 03/24942, WO 03/22871, WO 03/15775, WO 03/04498, WO 03/04496, WO 03/02530, WO 03/02596, WO 03/02595, WO 03/02593, WO 03/02553, WO 03/02531, WO 03/00181, WO 03/00180, WO 03/00250, WO 02/83109, WO 02/83128, WO 02/76450, WO 02/68420, WO 02/62764, WO 02/55088, WO 02/51836, WO 02/38541, WO 02/34900, WO 02/30891, WO 02/30890, WO 02/14271, WO 02/02560, WO 01/97808, WO 01/96295, WO 01/81337, WO 01/81304, WO 01/68603, WO 01/55105, WO 01/52825, WO 01/34594, WO 00/71135, WO 00/69868, WO 00/56297, WO 00/56296, WO 00/34241, WO 00/23421, WO 00/10549, WO 99/67278, WO

99/62914, WO 99/61431, WO 99/56753, WO 99/25719, WO 99/16864, WO 98/50066, WO 98/50046, WO 98/19998, WO 98/18763, WO 97/40832, WO 95/29691, WO 95/15309, WO 93/10127, WO 93/08259, WO 91/16339, EP 1671649, EP 1667524, EP 1664031, EP 1659123, EP 1658066, EP 1638970, EP 1638968, EP 1638950, EP 1635818, EP 1627870, EP 1625122, EP 1624874, EP 1517907, EP 1513808, EP 1492777, EP 1490335, EP 1489088, EP 1480961, EP 1476435, EP 1476429, EP 1469873, EP 1465891, EP 1463727, EP 1461337, EP 1450794, EP 1446116, EP 1442049, EP 1441719, EP 1426366, EP 1412357, EP1406873, EP 1406872, EP 1406622, EP 1404675, EP 1399420, EP 1399471, EP 1399470, EP 1399469, EP 1399433, EP 1399154, EP 1385508, EP 1377288, EP 1355886, EP 1354882, EP 1338592, EP 1333025, EP 1323710, EP 1304327, EP 1301187, EP 1296974, EP 1280797, EP 1282600, EP 1261586, EP 1258476, EP 1254113, EP 1248604, EP 1245568, EP 1215207, EP 1228061, EP 1137635, EP 1123272, EP 1104293, EP 1082314, EP 1050540, EP 1043328, EP 0995440, EP 0980249, EP 0975359, EP 0731789, EP 0641347, EP 0610317, EP 0528858, CA 2466870, CA 2433090, CA 2339537, CA 2289125, CA 2289124, CA 2123128, DD 296075, DE 19834591, DE 19828113, DE 19823831, DE 19616486, DE 10333935, DE 10327439, DE 10256264, DE 10251927, DE 10238477, DE 10238470, DE 10238243, DE 10143840, FR 2824825, FR 2822826, JP2005507261, JP 2005505531, JP 2005502624, JP 2005500321, JP 2005500308, JP2005023038, JP 2004536115, JP 2004535445, JP 2004535433, JP 2004534836, JP 2004534815, JP 2004532220, JP 2004530729, JP 2004525929, JP 2004525179, JP 2004522786, JP 2004521149, JP 2004503531, JP 2004315496, JP 2004244412, JP 2004043429, JP 2004035574, JP 2004026820, JP 2004026678, JP 2004002368, JP 2004002367, JP 2003535898, JP 2003535034, JP 2003531204, JP 2003531191, JP 2003531118, JP 2003524591, JP 2003520849, JP 2003327532, JP 2003300977, JP 2003238566, JP 2002531547, JP 2002527504, JP 2002517401, JP 2002516318, JP 2002363157, JP 2002356472, JP 2002356471, JP 2002265439, JP 2001510442, JP 2000511559, JP 2000327689, JP 2000191616, JP 1998182613, JP 1998081666, JP 1997509921, JP 1995501078, JP 1993508624, the disclosure of each of which is herein incorporated by reference in its entirety.

In one aspect of the present invention, the DPP-IV inhibitor is valine-pyrrolidide (Deacon et al, Diabetes (1998) 47:764769; the disclosure of which is herein incorporated by reference in its entirety).

In one aspect of the present invention, the DPP-IV inhibitor is 3-(L-Isoleucyl)thiazolidine (isoleucine-thiazolidide). Isoleucine-thiazolidide may be found in JP 2001510442, WO 97/40832, US 6,303,661, and DE 19616486, the disclosure of each of which is herein incorporated by reference in its entirety. Isoleucine-thiazolidide is described as an orally active and selective DPP-IV inhibitor [Pederson et al, Diabetes (1998) 47:1253-1258; the disclosure of which is herein incorporated by reference in its entirety].

In one aspect of the present invention, the DPP-IV inhibitor is 1-[2-[5-cyanopyridin-2-yl)amino]ethylamino]acetyl-2-cyano-(S)-pyrrolidine (NVP-DPP728). NVP-DPP728 may be found in

WO 98/19998 and JP 2000511559, the disclosure of each of which is herein incorporated by reference in its entirety. NVP-DPP728 is described as an orally active and selective DPP-IV inhibitor [Villhauer et al, J Med Chem (2002) 45:2362-2365].

In one aspect of the present invention, the DPP-IV inhibitor is 3(R)-Amino-1-[3-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrazin-7-yl]-4-(2,4,5-trifluorophenyl)butan-1-one (MK-0431; sitagliptin). MK-0431 may be found in EP 1412357, WO 03/04498, US 6,699,871, and US 2003100563, the disclosure of each of which is herein incorporated by reference in its entirety. MK-0431 is described as an orally active and selective DPP-IV inhibitor [Weber et al, Diabetes (2004) 53(Suppl.2):A151, 633-P (Abstract), the disclosure of which is herein incorporated by reference in its entirety].

In one aspect of the present invention, the DPP-IV inhibitor is (1-[[3-hydroxy-1-adamantyl)amino]acetyl]-2-cyano-(S)-pyrrolidine (LAF237; vildagliptin). LAF237 may be found in US 6,166,063, WO 00/34241, EP 1137635, and JP 2002531547, the disclosure of each of which is herein incorporated by reference in its entirety. LAF237 is described as an orally active and selective DPP-IV inhibitor [Villhauer et al, J Med Chem (2003) 46:2774-2789].

In one aspect of the present invention, the DPP-IV inhibitor is (1S,3S,5S)-2-[2(S)-Amino-2-(3-hydroxyadamantan-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile (BMS-477118; saxagliptin).

In one aspect of the present invention, the DPP-IV inhibitor is [1-[2(S)-Amino-3-methylbutyryl]pyrrolidin-2(R)-yl]boronic acid (PT-100).

In one aspect of the present invention, the DPP-IV inhibitor is GSK-823093.

In one aspect of the present invention, the DPP-IV inhibitor is PSN-9301.

In one aspect ot the present invention, the DPP-IV inhibitor is T-6666.

In one aspect of the present invention, the DPP-IV inhibitor is SYR-322 (alogliptin).

In one aspect of the present invention, the DPP-IV inhibitor is SYR-619.

In one aspect of the present invention, the DPP-IV inhibitor is CR-14023.

In one aspect of the present invention, the DPP-IV inhibitor is CR-14025.

In one aspect of the present invention, the DPP-IV inhibitor is CR-14240.

In one aspect of the present invention, the DPP-IV inhibitor is CR-13651.

In one aspect of the present invention, the DPP-IV inhibitor is NNC-72-2138.

In one aspect of the present invention, the DPP-IV inhibitor is NN-7201.

In one aspect of the present invention, the DPP-IV inhibitor is PHX-1149.

In one aspect of the present invention, the DPP-IV inhibitor is PHX-1004.

In one aspect of the present invention, the DPP-IV inhibitor is SNT-189379.

In one aspect of the present invention, the DPP-IV inhibitor is GRC-8087.

In one aspect of the present invention, the DPP-IV inhibitor is PT-630.

In one aspect of the present invention, the DPP-IV inhibitor is SK-0403.

In one aspect of the present invention, the DPP-IV inhibitor is GSK-825964.

In one aspect of the present invention, the DPP-IV inhibitor is TS-021.

In one aspect of the present invention, the DPP-IV inhibitor is GRC-8200.

In one aspect of the present invention, the DPP-IV inhibitor is GRC-8116.

In one aspect of the present invention, the DPP-IV inhibitor is FE107542.

In one aspect of the present invention, the DPP-IV inhibitor is (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-A]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine.

In one aspect of the present invention, the DPP-IV inhibitor is sitagliptin.

In one aspect of the present invention, the DPP-IV inhibitor is Januvia™ (sitagliptin phosphate).

In one aspect of the present invention, the DPP-IV inhibitor is (3R)-4-[(3R)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(2,2,2-trifluoroethyl)-1,4-diazepan-2-one.

In one aspect of the present invention, the DPP-IV inhibitor is selected from the right column of Table D. It is expressly contemplated that each individual DPP-IV inhibitor from the right column of Table D is a separate embodiment within the scope of the present invention.

In one aspect of the present invention, the DPP-IV inhibitor is selected from any set of compounds selected from the right column of Table D.

In one aspect of the present invention, the DPP-IV inhibitor is a compound of Formula (**XIX**).

In one aspect of the present invention, the DPP-IV inhibitor is a compound of Formula (**XX**).

In one aspect of the present invention, the DPP-IV inhibitor is a compound of Formula (**XXI**).

In one aspect of the present invention, the DPP-IV inhibitor is a compound of Formula (**XXII**).

In one aspect of the present invention, the DPP-IV inhibitor is a compound selected from Group S1, Group T1, Group V1, or Group V2.

In one aspect of the present invention, the DPP-IV inhibitor is identical to a compound disclosed in International Application No. PCT/US02/21349 (published as WO 03/004498).

In one aspect of the present invention, the DPP-IV inhibitor is identical to a compound disclosed in International Application No. PCT/EP99/09708 (published as WO 00/34241).

In one aspect of the present invention, the DPP-IV inhibitor is identical to a compound disclosed in International Application No. PCT/US01/07151 (published as WO 01/68603).

In one aspect of the present invention, the DPP-IV inhibitor is identical to a compound disclosed in International Application No. PCT/US2004/042209 (published as WO 2005/095381).

In one aspect of the present invention, the DPP-IV inhibitor has an IC_{50} of less than about 10 μM, less than about 1 μM, less than about 100 nM, less than about 75 nM, less than about 50 nM, less than about 25 nM, less than about 20 nM, less than about 15 nM, less than about 10 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, or less than about 1

nM. In certain embodiments, the DPP-IV inhibitor has an IC_{50} of less than about 50 nM, less than about 25 nM, less than about 20 nM, less than about 15 nM, less than about 10 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, or less than about 1 nM.

In one aspect of the present invention, the DPP-IV inhibitor is a selective DPP-IV inhibitor, wherein the selective DPP-IV inhibitor has a selectivity for human plasma DPP-IV over one or more of PPCE, DPP-II, DPP-8 and DPP-9 of at least about 10-fold, and in particular embodiment of at least about 100-fold, and in further particular emodiment of at least about 1000-fold.

In one aspect of the present invention, the DPP-IV inhibitor is a small molecule.

In one aspect of the present invention, the DPP-IV inhibitor is orally active.

In one aspect of the present invention, the DPP-IV inhibitor is an inhibitor of human DPP-IV.

In one aspect of the present invention, any one or more DPP-IV inhibitor can be excluded from any embodiment of the present invention.

Combination of GPR119 Agonist and DPP-IV Inhibitor

By way of illustration and not limitation, an exemplary combination of GPR119 agonist and DPP-IV inhibitor in accordance with the present invention is provided by selecting a GPR119 agonist from the left column of Table D and a DPP-IV inhibitor from the right column of Table D. It is expressly contemplated that each individual combination of GPR119 agonist and DPP-IV inhibitor provided by selecting a GPR119 agonist from the left column of Table D and a DPP-IV inhibitor from the right column of Table D is a separate embodiment within the scope of the present invention.

TABLE D

GPR119 Agonist	DPP-IV Inhibitor
[6-(4-Benzenesulfonyl-piperidin-1-yl)-5-nitro-pyrimidin-4-yl]-(4-methanesulfonyl-phenyl)-amine	valine-pyrrolidide
{4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yl]-piperazin-1-yl}-acetic acid ethyl ester	3-(L-Isoleucyl)thiazolidine (isoleucine-thiazolidide)
(2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine	1-[2-[5-cyanopyridin-2-yl)amino]ethylamino]acetyl-2-cyano-(S)-pyrrolidine (NVP-DPP728)
6'-[4-(2-Methoxycarbonyl-acetyl)-phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester	3(R)-Amino-1-[3-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrazin-7-yl]-4-(2,4,5-trifluorophenyl)butan-1-one (MK-0431; sitagliptin)

1-[4-(4-Acetyl-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-6'-yloxy)-phenyl]-ethanone	(1-[[3-hydroxy-1-adamantyl)amino]acetyl]-2-cyano-(S)-pyrrolidin (LAF237; vildagliptin)
6'-[4-(4-Hydroxy-benzenesulfonyl)-phenoxy]-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester	(1S,3S,5S)-2-[2(S)-Amino-2-(3-hydroxyadamantan-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile (BMS-477118; saxagliptin)
1-[5-(4-Benzoyl-phenoxy)-2-nitro-phenyl]-piperidine-4-carboxylic acid ethyl ester	[1-[2(S)-Amino-3-methylbutyryl]pyrrolidin-2(R)-yl]boronic acid (PT-100)
1-{5-[4-(2-Methoxycarbonyl-acetyl)-phenoxy]-2-nitro-phenyl}-piperidine-4-carboxylic acid ethyl ester	GSK-823093
1-[5-(2-Amino-4-ethanesulfonyl-phenoxy)-2-nitro-phenyl]-piperidine-4-carboxylic acid ethyl ester	PSN-9301
5-Bromo-1-[4-nitro-3-(4-propyl-piperidin-1-yl)-phenyl]-1H-pyridin-2-one	T-6666
6'-Benzenesulfonylamino-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester	SYR-322 (alogliptin)
6'-(Benzenesulfonyl-methyl-amino)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester	SYR-619
6'-(Benzenesulfonyl-butyl-amino)-3'-nitro-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester	CR-14023
1-[5-(4-Benzoyl-phenylamino)-2-nitro-phenyl]-piperidine-4-carboxylic acid ethyl ester	CR-14025
{4-[4-Nitro-3-(4-propyl-piperidin-1-yl)-phenylamino]-phenyl}-phenyl-methanone	CR-14240

3-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxymethyl]-pyrrolidine-1-carboxylic acid tert-butyl ester	CR-13651
4-[5-Cyano-6-(6-methylsulfanyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	NNC-72-2138
4-[5-Cyano-6-(6-methanesulfonyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	NN-7201
4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	PHX-1149
(4-Methanesulfonyl-phenyl)-[5-nitro-6-(piperidin-4-yloxy)-pyrimidin-4-yl]-amine	PHX-1004
1-{4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-yloxy]-piperidin-1-yl}-3,3-dimethyl-butan-1-one	SNT-189379
4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-ylamino]-piperidine-1-carboxylic acid tert-butyl ester	GRC-8087
N-(4-Methanesulfonyl-phenyl)-5-nitro-N'-piperidin-4-yl-pyrimidine-4,6-diamine	PT-630
1-{4-[6-(4-Methanesulfonyl-phenylamino)-5-nitro-pyrimidin-4-ylamino]-piperidin-1-yl}-ethanone	SK-0403
4-[6-(4-Cyano-2-fluoro-phenylamino)-5-ethynyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl	GSK-825964

ester	
4-[5-Ethynyl-6-(2-fluoro-4-[1,2,4]triazol-1-yl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	8-(3-Aminopiperidin-1-yl)-N2,7-dibenzyl-1-methylguanine trifluoroacetate
4-{5-Ethynyl-6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-pyrimidin-4-ylamino}-3-fluoro-benzonitrile	N-[2-[2-[8-(3-Aminopiperidin-1-yl)-7-(2-butynyl)-3-methylxanthin-1-yl]acetyl]phenyl]formamide
4-[5-Acetyl-6-(6-methanesulfonyl-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isobutyl ester	8-[3(R)-Aminopiperidin-1-yl]-7-(2-butynyl)-3-methyl-1-(quinazolin-2-ylmethyl)xanthine
1-[4-(1-Benzyl-azetidin-3-yloxy)-6-(6-methanesulfonyl-pyridin-3-ylamino)-pyrimidin-5-yl]-ethanone	8-(3-Aminopiperidin-1-yl)-1-(benzo[c]-1,8-naphthyridin-6-ylmethyl)-7-(2-butynyl)-3-methylxanthine
4-[5-Cyano-6-(6-propylamino-pyridin-3-ylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2-[8-[3(R)-Aminopiperidin-1-yl]-7-(2-butynyl)-3-methylxanthin-1-yl]-N-(2-pyridyl)acetamide
4-({[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-yl]-isopropyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester	2-(3-Aminopiperidin-1-yl)-3-(2-butynyl)-5-(quinoxalin-6-ylmethyl)-4,5-dihydro-3H-imidazo[4,5-d]pyridazin-4-one
4-(2-Fluoro-4-methanesulfonyl-phenoxy)-6-[1-(3-methoxy-propyl)-piperidin-4-yloxy]-5-methyl-pyrimidine	(1S,3S,5S)-2-[2(S)-Amino-4,4-dimethylpentanoyl]-2-azabicyclo[3.1.0]hexane-3(S)-carbonitrile trifluoroacetate
1-{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-3-methoxy-propan-2-ol	N1-(1-Cyanoethyl)-N1,3-dimethyl-L-valinamide
4-{6-[2-Fluoro-4-(5-isopropoxymethyl-[1,2,4]oxadiazol-3-yl)-phenoxy]-5-methyl-pyrimidin-4-yloxy}-piperidine-1-carboxylic acid isopropyl ester	(1S,3S,5S)-2-[2(S)-Amino-2-[1-(3,3-dimethylbutyryl)piperidin-4-yl]acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile
4-[6-(2-Fluoro-4-morpholin-4-yl-	2-[7-(2-Butynyl)-1-(2-phenylethyl)-8-(1-piperazinyl)xanthin-3-yl]-

phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	N-(2-propynyl)acetamide hydrochloride
{4-[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-[6-(2-pyrrolidin-1-yl-ethyl)-pyridin-3-yl]-methanone	2-[7-(2-Butynyl)-1-(3-cyanobenzyl)-6-oxo-8-(1-piperazinyl)-6,7-dihydro-1H-purin-2-yloxy]-N-methylbenzamide trifluoroacetate
(6-Amino-pyridin-3-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone	2-[3-(2-Butynyl)-4-oxo-2-(1-piperazinyl)-4,5-dihydro-3H-imidazo[4,5-d]pyridazin-5-ylmethyl]benzonitrile trifluoroacetate
4-({Cyclopropyl-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester	N-[1(S)-[2(S)-Cyanopyrrolidin-1-ylcarbonyl]-4-(pyrazin-2-ylcarboxamido)butyl]carbamic acid 1-acetoxyethyl ester
4-({Cyclopropyl-[6-(2-fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yl]-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester	2(S),4-Diamino-1-(4-thiomorpholinyl)butan-1-one
4-({[6-(2-Fluoro-4-methanesulfonyl-phenoxy)-5-methyl-pyrimidin-4-yl]-isopropyl-amino}-methyl)-piperidine-1-carboxylic acid isopropyl ester	1-[Perhydroindol-2(S)-ylcarbonyl]azetidine-2(S)-carbonitrile
4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-5-methyl-pyrimidin-4-ylsulfanyl]-piperidine-1-carboxylic acid isopropyl ester	1-(2-Benzothiazolyl)-1-[1-[(2S,3aS,7aS)-perhydroindol-2-ylcarbonyl]pyrrolidin-2(S)-yl]methanone hydrochloride
4-[1-(4-Methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	1-[2(S)-Amino-2-cyclohexylacetyl]-4-methylazetidine-2-carbonitril hydrochloride
4-[1-(4-Methanesulfonyl-phenyl)-3-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid	6-[2-[2-[5(S)-Cyano-4,5-dihydro-1H-pyrazol-1-yl]-2-oxoethylamino]ethylamino]pyridine-3-carbonitrile

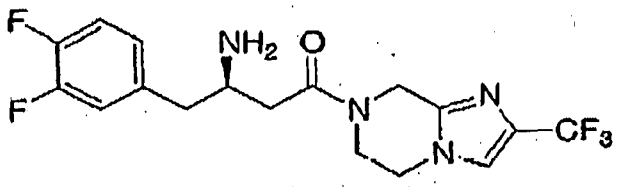
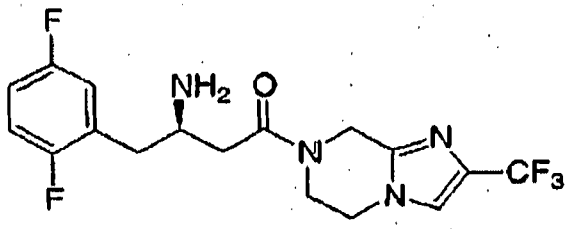
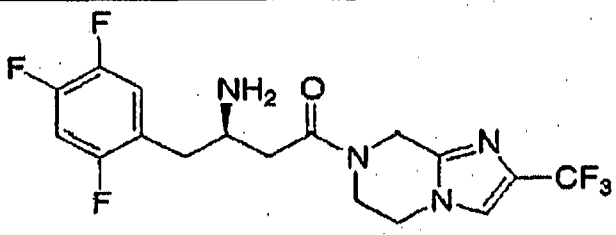
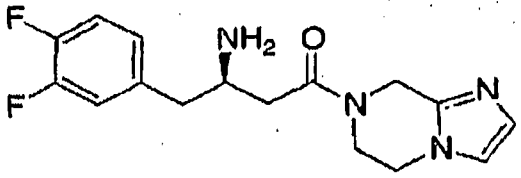
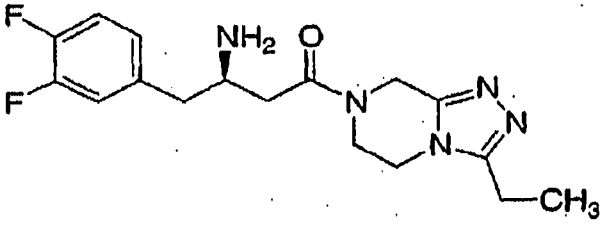
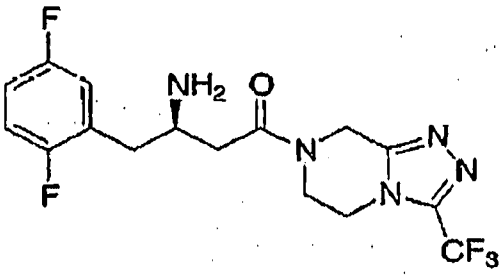
tert-butyl ester	
4-[1-(4-Methanesulfonyl-phenyl)-3,6-dimethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	6-[2-[2-[2(S)-Cyano-4(S)-fluoropyrrolidin-1-yl]-2-oxoethylamino]2-methylpropylamino]-N,N-dimethylpyridine-3-sulfonamide
4-({[1-(2,5-Difluoro-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-methyl-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester	trans-N-[4-[1(S)-Amino-2-[3(S)-fluoropyrrolidin-1-yl]-2-oxoethyl]cyclohexyl]-2,4-difluorobenzenesulfonamide
2-{4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-(4-trifluoromethoxy-phenyl)-ethanone	2(S)-Amino-1-(1-pyrrolidinyl)-2-[4-(thiazol-2-ylamino)cyclohexyl]ethanone trifluoroacetate
2-{4-[1-(2-Fluoro-4-methanesulfonyl-phenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy]-piperidin-1-yl}-1-(3-fluoro-phenyl)-ethanone	N-[(1R,3R)-3-[1(S)-Amino-2-oxo-2-(1-pyrrolidinyl)ethyl]cyclopentyl]-4-(methylsulfonyl)benzenesulfonamide
4-[9-(6-Methanesulfonyl-pyridin-3-yl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isobutyl ester	3(R)-Amino-1-(6-benzyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazin-7-yl)-4-(3,4-difluorophenyl)butan-1-one
{4-[9-(6-Methanesulfonyl-pyridin-3-yl)-9H-purin-6-yloxy]-piperidin-1-yl}-pyridin-3-yl-methanone	trans-N-[4-[1(S)-Amino-2-oxo-2-(1-pyrrolidinyl)ethyl]cyclohexyl]-2,4-difluorobenzenesulfonamide
4-[9-(4-Methanesulfonyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	3(R)-Amino-4-(2,5-difluorophenyl)-1-[4-hydroxy-2-(trifluoromethyl)-5,6,7,8-tetrahydropyrido[3,4-d]pyrimidin-7-yl]butan-1-one
4-[9-(2-Fluoro-4-propionylsulfamoyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester	N-[(1R,3R)-3-[1(S)-Amino-2-oxo-2-(1-pyrrolidinyl)ethyl]cyclopentyl]-2-(methylsulfonamido)ethanesulfonamide
4-[9-(4-Cyano-2-fluoro-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2-[4-[3(R)-Amino-4-(2-fluorophenyl)butyryl]-3(R)-benzylpiperazin-1-yl]-N-[3-(methylsulfonamido)phenyl]acetamide
4-[9-(2-Fluoro-4-sulfamoyl-phenyl)-9H-purin-6-yloxy]-piperidine-1-carboxylic acid isopropyl ester	3(R)-Amino-1-(3-thiazolidinyl)-4-(2,4,5-trifluorophenyl)butan-1-one
4-[3-(4-Methanesulfonyl-phenyl)-3H-	4-[3(R)-Amino-4-(2,4,5-trifluorophenyl)butyryl]-3(R)-methyl-1,4-

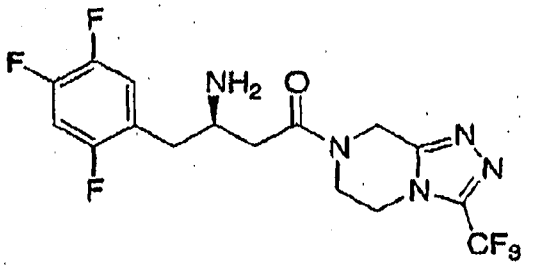
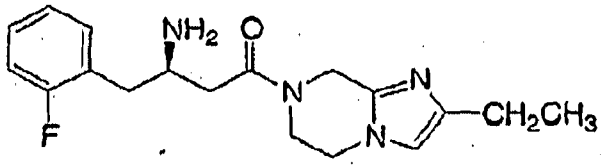
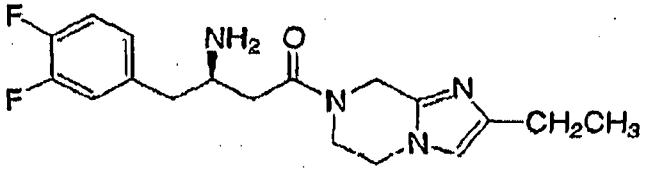
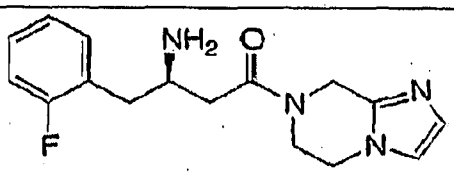
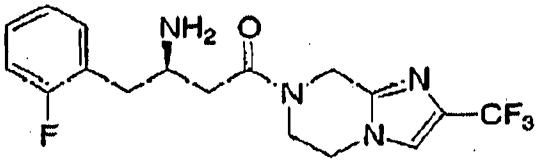
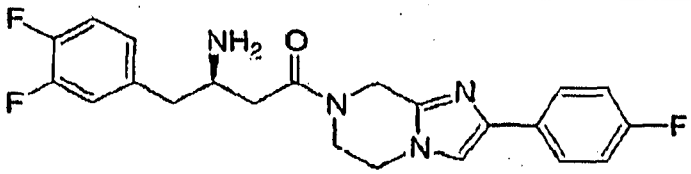
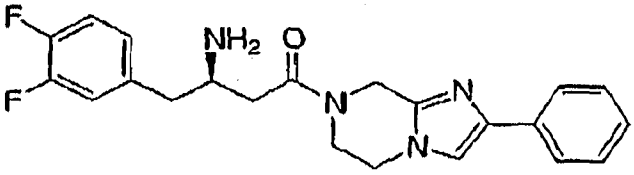
[1,2,3]triazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	diazepan-2-one
3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-3H-[1,2,3]triazolo[4,5-d]pyrimidine	3(S)-Amino-4-(3,3-difluoropyrrolidin-1-yl)-N,N-dimethyl-4-oxo-2(S)-[4-([1,2,4]triazolo[1,5-a]pyridin-6-yl)phenyl]butyramide
3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide	3(R)-Amino-1-[2-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyrazine-7-yl]-4-(2,4,5-trifluorophenyl)butanone hydrochloride
3-Fluoro-4-{7-[1-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl}-benzonitrile	2(S)-Amino-3(S)-(4-fluorophenyl)-1-(3-thiazolidinyl)butan-1-one
4-[3-(4-Methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	7-[3(R)-Amino-4-(2,5-difluorophenyl)butyryl]-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxylic acid ethyl ester
4-({Ethyl-[3-(4-methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-yl]-amino}-methyl)-piperidine-1-carboxylic acid tert-butyl ester	3(R)-Amino-1-(8-chloro-1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazol-2-yl)-4-(2,5-difluorophenyl)butan-1-one trifluoroacetate
4-[3-(4-Methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-ylsulfanyl]-piperidine-1-carboxylic acid tert-butyl ester	3(R)-Amino-4-(2,5-difluorophenyl)-1-[2-(4-fluorophenyl)-4,5,6,7-tetrahydrothiazolo[4,5-c]pyridin-5-yl]butan-1-one
4-[3-(4-Methanesulfonyl-phenyl)-isoxazolo[4,5-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2-[4-[2-[3(R)-Amino-4-(2-fluorophenyl)butyryl]-1,2,3,4-tetrahydroisoquinolin-3-ylcarboxamidomethyl]phenyl]acetic acid
4-[8-(2-Fluoro-4-methanesulfonyl-phenyl)-[1,7]naphthyridin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	3(S)-Amino-2-oxopiperidin-1-ylphosphonic diamide hydrochloride

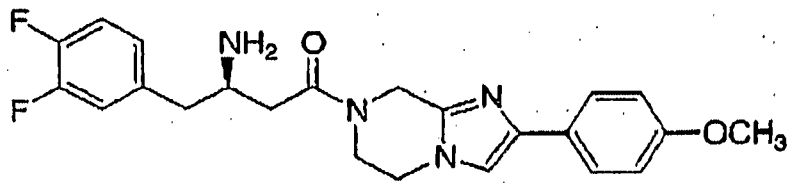
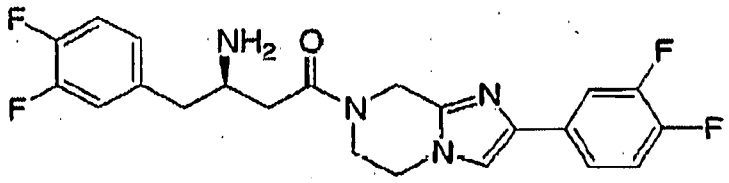
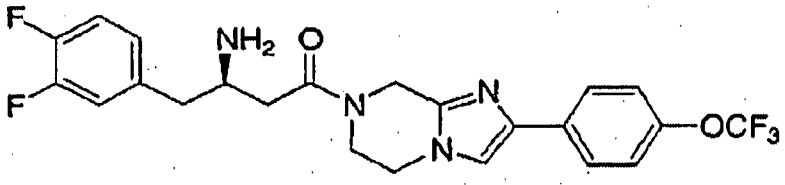
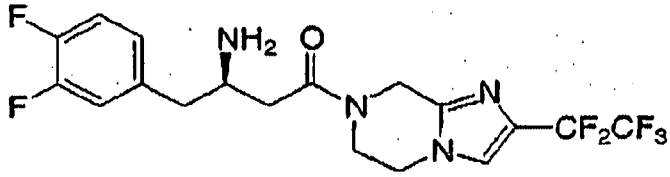
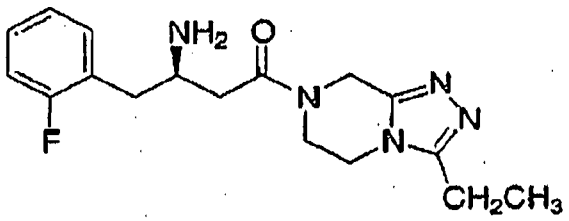
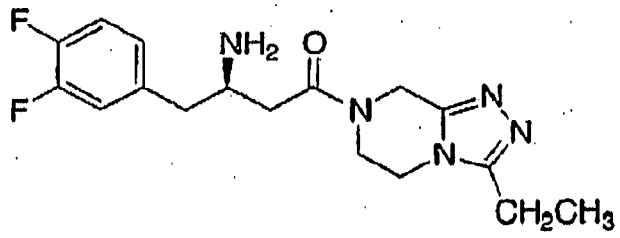
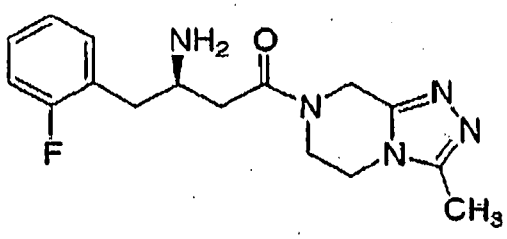
4-[8-(2-Fluoro-4-methanesulfonyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2-[2-(5-Nitropyridin-2-ylamino)ethylamino]-1-(1-pyrrolidinyl)ethanone dihydrochloride
4-[8-(4-Methylsulfanyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2-[8-(3-Aminopiperidin-1-yl)-1,3-dimethylxanthin-7-ylmethyl]benzonitrile hemisuccinate
4-[8-(4-Methanesulfonyl-phenyl)-quinolin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2(S)-Amino-2-cyclohexyl-1-(3,3,4,4-tetrafluoropyrrolidin-1-yl)ethanone hydrochloride
4-[8-(2-Fluoro-4-methanesulfonyl-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2(S)-Amino-2-cyclohexyl-1-(3-fluoropyrrolidin-1-yl)ethanone
4-[8-(2-Fluoro-4-propionylsulfamoyl-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	2-Amino-1-cyclopentyl-3-methylpentan-1-one hydrochloride
4-[8-(4-Cyano-2-fluoro-phenyl)-pyrido[3,4-d]pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	4-Amino-5-oxo-5-(1-pyrrolidinyl)pentanamide
3-(2-Fluoro-4-methanesulfonyl-phenyl)-7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidine	1-[2-[1,1-Dimethyl-2-(6-phenylpyridin-2-ylamino)ethylamino]acetyl]pyrrolidine-2(S)-carbonitrile hydrochloride
3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-N-propionyl-benzenesulfonamide	(7R*,8S*,13bS*)-7-Butyl-11,12-dimethoxy-,3,4,4a,6,7,8,9,9a,13b-decahydro-1H-pyrido[1,2-f]phenanthridin-8-amine
3-Fluoro-4-{7-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-cyclohexyloxy]-pyrazolo[1,5-a]pyrimidin-3-yl}-benzonitrile	5-(Aminomethyl)-6-(2,4-dichlorophenyl)-2-(3,5-dimethoxyphenyl)pyrimidin-4-amine
4-[3-(2-Fluoro-4-methanesulfonyl-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-	3-(Aminomethyl)-4-(2,4-dichlorophenyl)-7,8-dimethoxy-5H-indeno[1,2-b]pyridin-2-amine

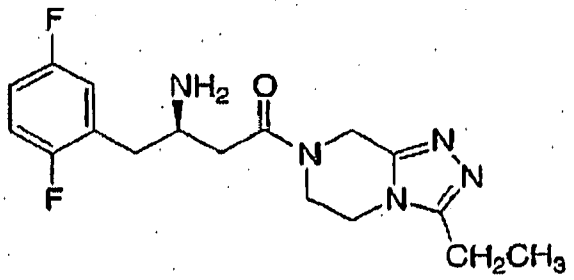
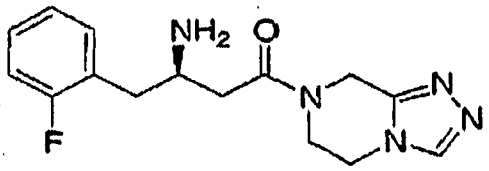
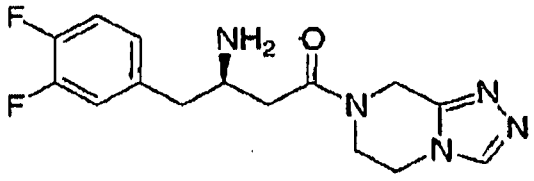
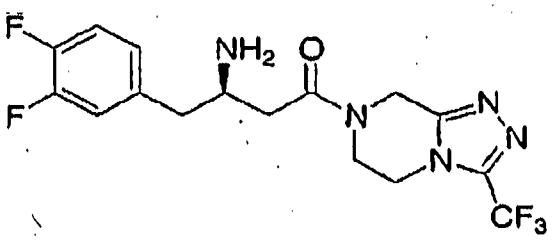
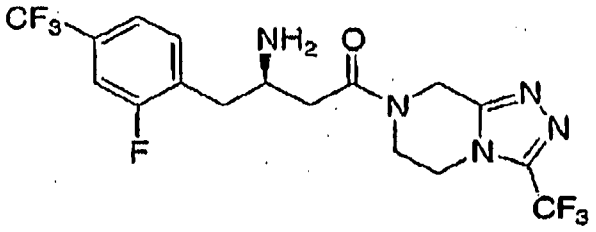
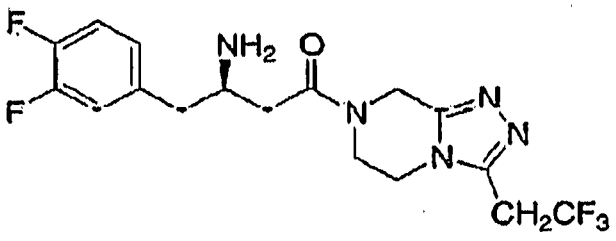
carboxylic acid isopropyl ester	
4-[3-(2-Fluoro-4-propionylsulfamoyl-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester	5-(Aminomethyl)-6-(2,4-dichlorophenyl)-N2-(2-methoxyethyl)-N2 methylpyrimidine-2,4-diamine
4-[3-(4-Cyano-2-fluoro-phenyl)-1-methyl-1H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester	4,4-Difluoro-1-[2-[exo-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3 ylamino]acetyl]pyrrolidine-2(S)-carbonitrile
4-[3-(2-Fluoro-4-methanesulfonyl-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester	exo-3-[2-[8-(2-Pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-ylamino]acetyl]thiazolidine-4(R)-carbonitrile
4-[3-(2-Fluoro-4-propionylsulfamoyl-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester	1-[2-[3-(2,3-Dihydro-1H-isoindol-2-yl)-1,1-dimethyl-3-oxopropylamino]acetyl]pyrrolidine-2(S)-carbonitrile
4-[3-(4-Cyano-2-fluoro-phenyl)-2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yloxy]-piperidine-1-carboxylic acid isopropyl ester	8-(3-Aminoperhydroazepin-1-yl)-3-methyl-7-(2-methylbenzyl)-2,3,6,7-tetrahydro-1H-purine-2,6-dione
4-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-6-(4-methanesulfonyl-phenoxy)-pyrimidine	8-[3(R)-Aminopiperidin-1-yl]-7-(5-fluoro-2-methylbenzyl)-1,3-dimethylxanthine
{6-[4-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-pyrimidin-4-yl}-(4-methanesulfonyl-phenyl)-amine	2-[2-(3-Aminopiperidin-1-yl)-6,7-dimethoxy-4-oxo-3,4-dihydroquinazolin-3-ylmethyl]benzonitrile
4-{[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yl]-methyl-amino}-piperidine-1-carboxylic acid tert-butyl ester	1-[2(S)-Amino-3,3-dimethylbutyryl]-4(S)-fluoropyrrolidine-2(S)-carbonitrile hydrochloride
4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid tert-butyl ester	2-[3-(Aminomethyl)-4-butoxy-2-(2,2-dimethylpropyl)-1-oxo-1,2-dihydroisoquinolin-6-yloxy]acetamide hydrochloride
(2-Fluoro-4-methanesulfonyl-phenyl)-	3-(3-Chloroimidazo[1,2-a]pyridin-2-ylmethylsulfonyl)-N,N-

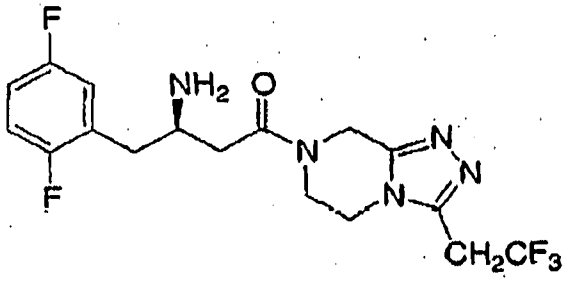
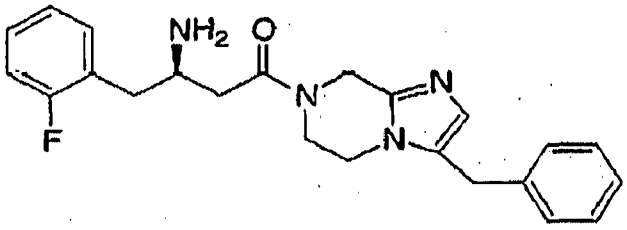
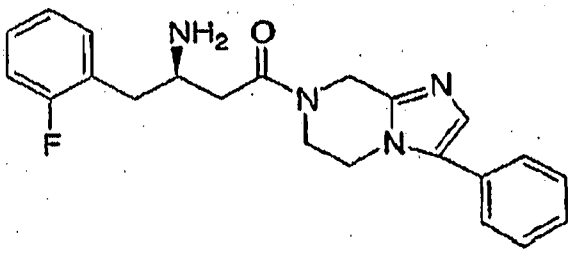
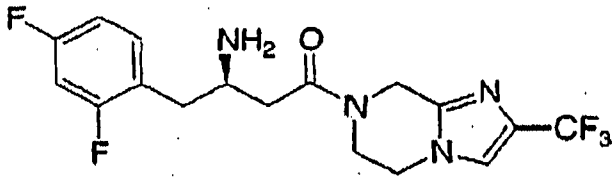
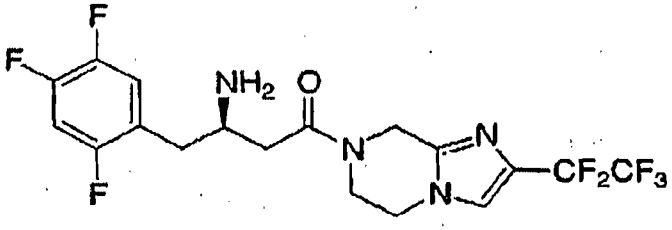
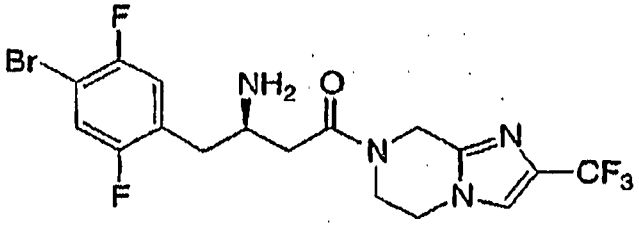
{6-[1-(3-isopropyl-[1,2,4]oxadiazol-5-ylmethyl)-piperidin-4-yloxy]-pyrimidin-4-yl}-amine; 4-[6-(2-Fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	dimethyl-1H-1,2,4-triazole-1-carboxamide
(6-Chloro-pyridin-2-yl)-{4-[6-(2-fluoro-4-methanesulfonyl-phenylamino)-pyrimidin-4-yloxy]-piperidin-1-yl}-methanone	6-Chloro-2-isobutyl-4-phenylquinolin-3-ylmethylamine
[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-methyl-amine	trans-1-[2-[4-(1,3-Dioxo-2,3-dihydro-1H-isoindol-2-yl)cyclohexylamino]acetyl]pyrrolidine-2(S)-carbonitrile hydrochloride
[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-p-tolyl-amine	trans-4-[2-[4(R)-Cyanothiazolidin-3-yl]-2-oxoethylamino]-N,N-dimethylcyclohexanecarboxamide hydrochloride
[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-(4-methoxy-phenyl)-amine	N-(5-Chloropyridin-2-yl)-2-[4-[1-[2-(4-cyanothiazolidin-3-yl)-2-oxoethyl]hydrazino]piperidin-1-yl]acetamide tris(trifluoroacetate)
[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-phenyl-amine	6-[2-[2-[2(S)-Cyanoazetidin-1-yl]-2-oxoethylamino]ethylamino]pyridine-3-carbonitrile dihydrochloride
[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-cyclohexyl-amine	4(S)-Fluoro-1-[2-[1-(2-hydroxyacetyl)-4-methylpiperidin-4-ylamino]acetyl]pyrrolidine-2(S)-carbonitrile fumarate
5-[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-ylamino]-pentan-1-ol	TS-021
3-[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-ylamino]-propionitrile	GRC-8200
[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-yl]-(4-fluoro-benzyl)-amine	GRC-8116
[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-yl]-[2-(4-chloro-phenyl)-ethyl]-amine	FE107542

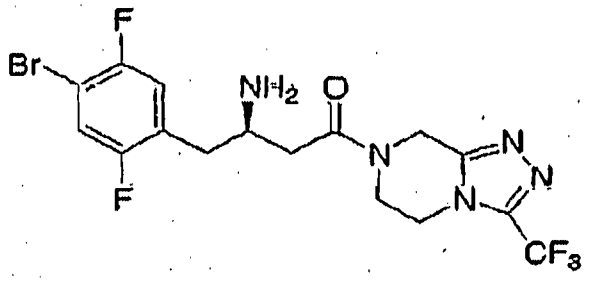
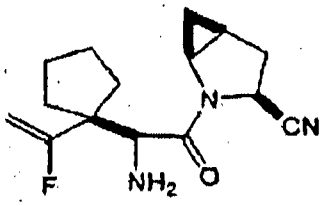
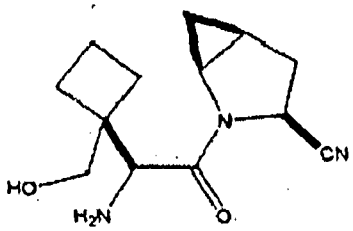
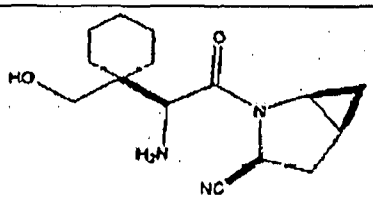
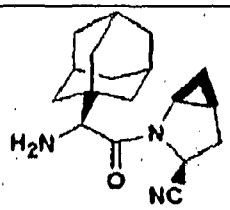
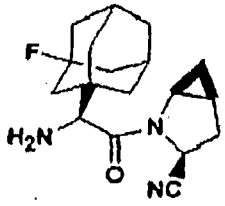
[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-yl]-pyridin-2-ylmethyl-amine	
[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-pyridin-3-ylmethyl-amine	
3-{[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-ylamino]-methyl}-1H-pyridin-2-one	
4-{[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-ylamino]-methyl}-1H-pyridin-2-one	
4-{2-[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one	
[2-(3-Chloro-4-fluoro-phenyl)-6-ethyl-pyrimidin-4-yl]-(1,1-dioxo-hexahydro-1l6-thiopyran-4-yl)-amine	

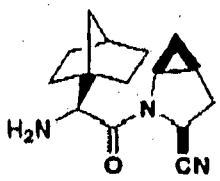
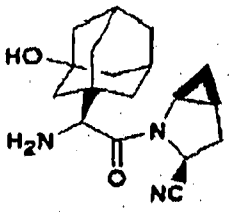
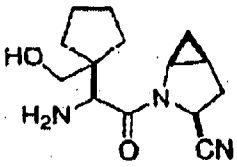
[6-Methyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-yl]-[2-(1-oxy-pyridin-3-yl)-ethyl]-amine	
[6-Ethyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-yl]-[2-(1-oxy-pyridin-3-yl)-ethyl]-amine	
[6-Methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-yl]-[2-(1-oxy-pyridin-3-yl)-ethyl]-amine	
4-{4-Methyl-6-[2-(1-oxy-pyridin-3-yl)-ethylamino]-pyrimidin-2-yl}-benzonitrile	
2-[4-(6-Methyl-2-phenyl-pyrimidin-4-ylamino)-phenyl]-ethanol	
[2-(3-Chloro-phenyl)-6-methyl-pyrimidin-4-yl]-methyl-amine	
2-{[2-(4-Bromo-phenyl)-6-methyl-pyrimidin-4-yl]-methyl-amino}-ethanol; compound with methane	

3-[6-Ethyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-propane-1,2-diol	
(*S*)-3-[6-Methyl-2-(2,3,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-propane-1,2-diol	
(*S*)-3-[2-(4-Bromo-3-fluoro-phenyl)-6-methyl-pyrimidin-4-ylamino]-propane-1,2-diol	
(*R*)-3-[6-Ethyl-2-(3,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-propane-1,2-diol	
(*R*)-3-[2-(3-Chloro-4-fluoro-phenyl)-6-ethyl-pyrimidin-4-ylamino]-propane-1,2-diol	
(*R*)-3-[2-(4-Bromo-2,5-difluoro-phenyl)-5-fluoro-6-methyl-pyrimidin-4-ylamino]-propane-1,2-diol	
(*R*)-3-[2-(4-Chloro-2,5-difluoro-phenyl)-6-difluoromethyl-pyrimidin-4-ylamino]-propane-1,2-diol	

5-{2-[2-(4-Bromo-phenyl)-6-ethyl-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one	
5-{2-[6-Methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one	
4-{2-[2-(4-Chloro-2,5-difluoro-phenyl)-6-ethyl-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one	
6-Chloro-4-{2-[6-methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one	
4-{1-Hydroxy-2-[6-methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one	
4-{1-Methyl-2-[6-methyl-2-(2,4,5-trifluoro-phenyl)-pyrimidin-4-ylamino]-ethyl}-1H-pyridin-2-one	

4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid *tert*-butyl ester	
4-[5-(2-Cyanopyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethoxy]piperidine-1-carboxylic acid *tert*-butyl ester	
4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid cyclopentyl ester	
4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)piperidine-1-carboxylic acid 2,2,2-trichloroethyl ester	
4-[Ethyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid *tert*-butyl ester	
4-[Methyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]piperidine-1-carboxylic acid cyclopentyl ester	

4-{[Methyl-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethyl)amino]methyl}piperidine-1-carboxylic acid 2,2,2-trichloroethyl ester	
4-[5-(4-Butyl-cyclohexyl)-[1,2,4]oxadiazol-3-yl]-pyridine (PSN375963)	
4-(3-Pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)-piperidine-1-carboxylic acid tert-butyl ester (PSN632408)	
4-[6-(6-Methanesulfonyl-2-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	
{6-[1-(3-Isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-4-yloxy]-5-methoxy-pyrimidin-4-yl}-(6-methanesulfonyl-2-methyl-pyridin-3-yl)-amine	
4-[6-(6-Methanesulfonyl-4-methyl-pyridin-3-ylamino)-5-methoxy-pyrimidin-4-yloxy]-piperidine-1-carboxylic acid isopropyl ester	

4-{[Methyl-(2-pyridin-4-ylpyrimidin-4-yl)-amino]methyl}piperidine-1-carboxylic acid tert-butyl ester	
4-{[Methyl-(2-pyridin-4-ylpyrimidin-4-ylmethyl)amino]methyl}piperidine-1-carboxylic acid tert-butyl ester	
4-[([2,4']Bipyridinyl-6-ylmethylmethylamino)methyl]piperidine-1-carboxylic acid tert-butyl ester	
	(2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-A]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine
	(3R)-4-[(3R)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(2,2,2-trifluoroethyl)-1,4-diazepan-2-one

Additionally, compounds of the invention, including those illustrated in Table D, encompass all pharmaceutically acceptable salts, solvates, and hydrates thereof. *See*, e.g., Berge et al (1977), Journal of Pharmaceutical Sciences 66:1-19; and Polymorphism in Pharmaceutical Solids (1999) Brittain, ed., Marcel Dekker, Inc.; the disclosure of each of which is herein incorporated by reference in its entirety.

Composition/Formulation and Methods of Treatment

A GPR119 agonist optionally in combination with a DPP-IV inhibitor according to the present invention and including the combination therapy relating to a GPR119 agonist in combination with a DPP-IV inhibitor described above can be formulated into pharmaceutical compositions and medicaments for use in accordance with the present invention using techniques well known in the art. Proper formulation is dependent on the route of administration chosen.

As relates to therapies of the present invention, namely therapies relating to a GPR119 agonist optionally in combination with a DPP-IV inhibitor and including the combination therapy relating to a GPR119 agonist and a DPP-IV inhibitor described above, the compounds according to the invention can be administered in any suitable way. Suitable routes of administration include oral, nasal, rectal, transmucosal, transdermal, or intestinal administration, parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous,

intraperitoneal, intranasal, intrapulmonary (inhaled) or intraocular injections using methods known in the art. Other suitable routes of administration are aerosol and depot formulation. Sustained release formulations, particularly depot, of the invented medicaments are expressly contemplated. In certain preferred embodiments, the compounds according to the present invention are administered orally. The compounds according to the present invention can be made up in solid or liquid form, such as tablets, capsules, powders, syrups, elixirs and the like, aerosols, sterile solutions, suspensions or emulsions, and the like. In certain embodiments, one or both of the GPR119 agonist and the DPP-IV inhibitor are administered orally.

Formulations for oral administration may be in the form of aqueous solutions and suspensions, in addition to solid tablet and capsule formulations. The aqueous solutions and suspensions may be prepared from sterile powders or granules. The compounds may be dissolved in water, polyethylene glycol, propylene glycol, ethanol, corn oil, cottonseed oil, peanut oil, sesame oil, benzyl alcohol, sodium chloride, and/or various buffers. Other adjuvants are well and widely known in the art.

It will be appreciated that the GPR119 agonist and the DPP-IV inhibitor may be present as a combined preparation for simultaneous, separate or sequential use for the treatment or prevention of a condition characterized by low bone mass, such as osteoporosis, and for increasing bone mass in an individual. Such combined preprations may be, for example, in the form of a twin pack.

It will therefore be further appreciated that the invention contemplates a product comprising or consisting essentially of a GPR119 agonist and a DPP-IV inhibitor as a combined preparation for simultaneous, separate or sequential use in the treatment or prevention of a condition characterized by low bone mass, such as osteoporosis, and for increasing bone mass in an individual.

A combination of the present invention comprising or consisting essentially of a GPR119 agonist and a DPP-IV inhibitor can be prepared by mixing the GPR119 agonist and the DPP-IV inhibitor either all together or independently with a pharmaceutically acceptable carrier, excipient, binder, diluent, etc. as described herein, and administering the mixture or mixtures either orally or non-orally as a pharmaceutical composition(s).

It will therefore be further appreciated that the GPR119 agonist and the DPP-IV inhibitor or pharmaceutical composition can be administered in separate dosage forms or in a single dosage form.

It is further appreciated that when the GPR119 agonist and the DPP-IV inhibitor are in separate dosage forms, GPR119 agonist and DPP-IV inhibitor can be administered by different routes.

Pharmaceutical compositions of the GPR119 agonist and DPP-IV inhibitor, either individually or in combination, may be prepared by methods well known in the art, e.g., by means of conventional mixing, dissolving, granulation, dragee-making, levigating, emulsifying, encapsulating, entrapping, lyophilizing processes or spray drying.

Pharmaceutical compositions for use in accordance with the present invention may be formulated in conventional manner using one or more physiologically acceptable carriers comprising

excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. Suitable pharmaceutically acceptable carriers are available to those in the art [*see*, e.g., Remington: The Science and Practice of Pharmacy, (Gennaro et al., eds.), 20th Edition, 2000, Lippincott Williams & Wilkins; and Handbook of Pharmaceutical Excipients (Rowe et al., eds), 4th Edition, 2003, Pharmaceutical Press; the disclosure of each of which is herein incorporated by reference in its entirety]. Proper formulation is dependent upon the route of administration chosen. The term "carrier" material or "excipient" material herein means any substance, not itself a therapeutic agent, used as a carrier and/or diluent and/or adjuvant, or vehicle for delivery of a therapeutic agent to a subject or added to a pharmaceutical composition to improve its handling or storage properties or to permit or facilitate formation of a dose unit of the composition into a discrete article such as a capsule or tablet suitable for oral admininstration. Excipients can include, by way of illustration and not limitation, diluents, disintegrants, binding agents, adhesives, wetting agents, polymers, lubricants, glidants, substances added to mask or counteract a disagreeable taste or odor, flavors, dyes, fragrances, and substances added to improved appearance of the composition. Acceptable excipients include stearic acid, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulfuric acids, magnesium carbonate, talc, gelatin, acacia gum, sodium alginate, pectin, dextrin, mannitol, sorbitol, lactose, sucrose, starches, gelatin, cellulosic materials, such as cellulose esters of alkanoic acids and cellulose alkyl esters, low melting wax cocoa butter or powder, polymers, such as polyvinyl-pyrrolidone, polyvinyl alcohol, and polytheylene glycols, and other pharmaceutically acceptable materials. The components of the pharmaceutical composition can be encapsulated or tableted for convenient administration.

Pharmaceutically acceptable refers to those properties and/or substances which are acceptable to the patient from a pharmacological/toxicological point of view and to the manufacturing pharmaceutical chemist from a physical/chemical point of view regarding composition, formulation, stability, patient acceptance and bioavailability.

As relates to the combination therapy described above, when the GPR119 agonist and the DPP-IV inhibitor are in separate dosage forms, it is understood that a pharmaceutically acceptable carrier used for the GPR119 agonist formulation need not be identical to a pharmaceutically acceptable carrier used for the DPP-IV inhibitor formulation.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used which may optionally contain gum Arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical compositions which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with a filler such as lactose, a

binder such as starch, and/or a lubricant such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, liquid polyethylene glycols, cremophor, capmul, medium or long chain mono-, di- or triglycerides. Stabilizers may be added in these formulations, also.

Additionally, a GPR119 agonist and the combination of a GPR119 agonist with a DPP-IV inhibitor may be delivered using a sustained-release system. Various sustained-release materials have been established and are well known to those skilled in the art. Sustained-release tablets or capsules are particularly preferred. For example, a time delay material such as glyceryl monostearate or glyceryl distearate may be employed. The dosage form may also be coated by the techniques described in the U.S. Pat. Nos. 4,256,108, 4,166,452, and 4,265,874 to form osmotic therapeutic tablets for controlled release.

It is expressly contemplated that therapies of the present invention, namely therapies relating to a GPR119 agonist optionally in combination with a DPP-IV inhibitor and including the combination therapy relating to a GPR119 agonist and a DPP-IV inhibitor described above, may be administered or provided alone or in combination with one or more other pharmaceutically or physiologically acceptable compound. In one aspect of the present invention, the other pharmaceutically or physiologically acceptable compound is not a GPR119 agonist and is not a DPP-IV inhibitor. In one aspect of the present invention, the other pharmaceutically or physiologically acceptable compound is a pharmaceutical agent selected from the group consisting of calcium, vitamin D, estrogen, tibolone, selective estrogen receptor modulator (SERM; e.g., raloxifene, tamoxifen), biphosphonate (e.g., etidronate, alendronate, risedronate), calcitonin, 1α-hydroxylated metabolite of vitamin D, fluoride, thiazide, anabolic steroid, ipriflavone, vitamin K, parathyroid hormone (PTH), strontium, statin, osteoprotererin, EP4 receptor selective agonist, cannabinoid receptor type 2 (CB2) selective agonist, and p38 MAP kinase inhibitor. (See, e.g., World Health Organization Technical Report Series 921 (2003), Prevention and Management of Osteoporosis.)

In a combination therapy according to the present invention, the GPR119 agonist according to the present invention and the DPP-IV inhibitor according to the present invention can be administered simultaneously or at separate intervals. When administered simultaneously the GPR119 agonist and the DPP-IV inhibitor can be incorporated into a single pharmaceutical composition or into separate compositions, e.g., the GPR119 agonist in one composition and the DPP-IV inhibitor in another composition. Each of these compositions may be formulated with common excipients, diluents or carriers, and compressed into tablets, or formulated elixirs or solutions; and as sustained relief dosage forms and the like. The GPR119 agonist and DPP-IV inhibitor may be administered via different routes. For example, the GPR119 agonist may be administered orally via tablet and the DPP-IV inhibitor may be administered via inhalation.

When separately administered, therapeutically effective amounts of the GPR119 agonist and the DPP-IV inhibitor according to the present invention are administered on a different schedule. One

may be administered before the other as long as the time between the two administrations falls within a therapeutically effective interval. A therapeutically effective interval is a period of time beginning when one of either (a) the GPR119 agonist or (b) the DPP-IV inhibitor is administered to an individual and ending at the limit of the beneficial effect in the treatment of the combination of (a) and (b).

In one aspect, the present invention features a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and at least one pharmaceutically acceptable carrier.

In one aspect, the present invention features a combination comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention features a pharmaceutical combination comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier.

In one aspect, the present invention features a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist is in an amount sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual.

In one aspect, the present invention features a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual.

In one aspect, the present invention features a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and

an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, and wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in the individual.

In one aspect, the present invention features a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, and wherein the effect is a synergistic effect.

In one aspect, the present invention relates to a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention relates to a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, wherein the effect is a synergistic effect, and wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in the individual.

In one aspect, the present invention relates to a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and

an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention relates to a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, wherein the effect given by the combination of the amount of the GPR119 agonist and the amount of the DPP-IV inhibitor is greater than the effect given by the amount of the GPR119 agonist alone and the effect given by the amount of the DPP-IV inhibitor alone.

In one aspect, the present invention features a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist is in an amount sufficient to give an effect in increasing a GIP level in an individual.

In one aspect, the present invention features a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in increasing a GIP level in an individual.

In one aspect, the present invention features a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in increasing a GIP level in a subject, and wherein the amount of the

GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in increasing a GIP level in the individual.

In one aspect, the present invention features a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention features a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in increasing a GIP level in an individual, and wherein the effect is a synergistic effect.

In one aspect, the present invention relates to a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention relates to a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in increasing a GIP level in a subject, wherein the effect is a synergistic effect, and wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in increasing a GIP level in the individual.

In one aspect, the present invention relates to a composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In one aspect, the present invention relates to a pharmaceutical composition comprising or consisting essentially of a combination of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention, together with at least one pharmaceutically acceptable carrier. The present invention also relates to a dosage form of the composition or of the pharmaceutical composition wherein the GPR119 agonist and the DPP-IV inhibitor are in amounts sufficient to give an effect in increasing a GIP level in a subject, wherein the effect given by the combination of the amount of the GPR119 agonist and the amount of the DPP-IV inhibitor is greater than the effect given by the amount of the GPR119 agonist alone and the effect given by the amount of the DPP-IV inhibitor alone.

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an amount to achieve their intended purpose. In some

embodiments, a pharmaceutical composition of the present invention is understood to be useful for treating or preventing a condition characterized by low bone mass, such as osteoporosis, or for increasing bone mass in an individual. Conditions characterized by low bone mass are according to the present invention. In some embodiments, a pharmaceutical composition of the present invention is understood to be useful for increasing a GIP level in an individual. As relates to the present invention, determination of the amount of a GPR119 agonist or of the amount of a combination of a GPR119 agonist with a DPP-IV inhibitor sufficient to achieve an intended purpose according to the invention is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

The data obtained from animal studies, including but not limited to studies using mice, rats, rabbits, pigs, and non-human primates, can be used in formulating a range of dosage for use in humans. In general, one skilled in the art understands how to extrapolate *in vivo* data obtained in an animal model system to another, such as a human. In some circumstances, these extrapolations may merely be based on the weight of the animal model in comparison to another, such as a human; in other circumstances, these extrapolations are not simply based on weights but rather incorporate a variety of factors. Representative factors include the type, age, weight, sex, diet and medical condition of the patient, the severity of the disease, the route of administration, pharmacological considerations such as the activity, efficacy, pharmacokinetic and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized, on whether an acute or chronic disease state is being treated or prophylaxis is conducted or on whether further active compounds are administered in addition to the compounds of the present invention and as part of a drug combination. The dosage regimen for treating a disease condition with the compounds and/or compositions of this invention is selected in accordance with a variety factors as cited above. Thus, the actual dosage regimen employed may vary widely and therefore may deviate from a preferred dosage regimen and one skilled in the art will recognize that dosage and dosage regimen outside these typical ranges can be tested and, where appropriate, may be used in the methods of this invention.

An exemplary animal model system is the rat ovariectomy (OVX) bone loss model. The ovariectomized rat is an excellent preclinical animal model that correctly emulates the important clinical feature of the estrogen depleted human skeleton and the response of therapeutic agents. In this model, a therapeutic efficacy is achieved when the bone loss associated with ovariectomy is partially or completely prevented. (See, e.g., Bollag et al, Mol Cell Endocrinol (2001) 177:35-41; and Jee et al, J Musculoskel Neuron Interact (2001) 1:193-207.) In certain embodiments, therapeutic efficacy is achieved when the bone loss associated with ovariectomy is at least about 10% prevented, at least about 20% prevented, at least about 30% prevented, at least about 40% prevented, at least about 50% prevented, at least about 60% prevented, at least about 70% prevented, at least about 75% prevented, at least about 80% prevented, at least about 85% prevented, at least about 90% prevented, at least about 95% prevented, or 100% prevented.

An additional exemplary animal model system is increase of a blood GIP level after glucose challenge in mice. In certain embodiments, the blood GIP level is a plasma GIP level. In certain embodiments, the GIP level is a glucose-independent GIP level. In certain embodiments, the GIP level is a glucose-dependent GIP level. In certain embodiments, the GIP is total GIP. In certain embodiments, the total GIP is measured using a centrally or C-terminally directed assay. In certain embodiments, the GIP is bioactive GIP. In certain embodiments, the bioactive GIP is measured using an N-terminal-specific assay. In certain embodiments, the bioactive GIP has activity for promoting bone formation. In certain embodiments, therapeutic efficacy is achieved when the blood GIP level is increased by at least about 10%, at least about 25%, at least about 50%, at least about 100%, at least about 150%, at least about 200%, at least about 300%, at least about 400%, or at least about 500%.

Dosage amount and interval may be adjusted in order to provide an intended therapeutic effect. It will be appreciated that the exact dosage of a GPR119 agonist or DPP-IV inhibitor in accordance with the present invention will vary depending on the GPR119 agonist, the combination of a GPR119 agonist and a DPP-IV inhibitor, its potency, the mode of administration, the age and weight of the patient and the severity of the condition to be treated. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. By way of illustration and not limitation, an amount of a GPR119 agonist and/or an amount of a DPP-IV inhibitor in accordance with the present invention is less than about 0.001 mg/kg body weight, less than about 0.005 mg/kg body weight, less than about 0.01 mg/kg body weight, less than about 0.05 mg/kg body weight, less than about 0.1 mg/kg body weight, less than about 0.5 mg/kg body weight, less than about 1 mg/kg body weight, less than about 5 mg/kg body weight, less than about 10 mg/kg body weight, less than about 50 mg/kg body weight, or less than about 100 mg/kg body weight. In certain embodiments, an amount of a GPR119 agonist and/or an amount of a DPP-IV inhibitor in accordance with the present invention is less than about 0.001-100 mg/kg body weight, less than about 0.001-50 mg/kg body weight, less than about 0.001-10 mg/kg body weight, less than about 0.001-5 mg/kg body weight, less than about 0.001-1 mg/kg body weight, less than about 0.001 to 0.5 mg/kg body weight, less than about 0.001-0.1 mg/kg body weight, less than about 0.001-0.05 mg/kg body weight, less than about 0.001-0.01 mg/kg body weight, or less than about 0.001-0.005 mg/kg body weight.

It is expressly contemplated that a GPR119 agonist and a combination of a GPR119 agonist and a DPP-IV inhibitor can be used in methods of preventing bone loss (e.g., methods of preventing a decrease in bone mass), methods of inhibiting bone loss (e.g., methods of inhibiting a decrease in bone mass), methods of maintaining bone mass, and methods of promoting bone formation (e.g., methods of increasing bone mass) in an individual.

A preferred dosage range for an amount of a GPR119 agonist which can be administered on a daily or regular basis to achieve desired results is 0.001-100 mg/kg (mpk) body mass. Other preferred dosage range is 0.001-30 mg/kg body mass. Other preferred dosage range is 0.001-10 mg/kg body

mass. Other preferred dosage range is 0.001-3.0 mg/kg body mass. Other preferred dosage range is 0.001-1.0 mg/kg body mass. Other preferred dosage range is 0.001-0.3 mg/kg body mass. Other preferred dosage range is 0.001-0.1 mg/kg body mass. Other preferred dosage range is 0.001-0.03 mg/kg body mass. Other preferred dosage range is 0.001-0.01 mg/kg body mass. Of course, these daily dosages can be delivered or administered in small amounts periodically during the course of a day. It is noted that these dosage ranges are only preferred ranges and are not meant to be limiting to the invention.

A preferred dosage range for an amount of a GPR119 agonist used in combination with a DPP-IV inhibitor for which a combination can be administered on a daily or regular basis to achieve desired results is 0.001-100 mg/kg body mass. Other preferred dosage range is 0.001-30 mg/kg body mass. Other preferred dosage range is 0.001-10 mg/kg body mass. Other preferred dosage range is 0.001-3.0 mg/kg body mass. Other preferred dosage range is 0.001-1.0 mg/kg body mass. Other preferred dosage range is 0.001-0.3 mg/kg body mass. Other preferred dosage range is 0.001-0.1 mg/kg body mass. Other preferred dosage range is 0.001-0.03 mg/kg body mass. Other preferred dosage range is 0.001-0.01 mg/kg body mass. Of course, these daily dosages can be delivered or administered in small amounts periodically during the course of a day. It is noted that these dosage ranges are only preferred ranges and are not meant to be limiting to the invention.

A preferred dosage range for an amount of a DPP-IV inhibitor used in combination with a GPR119 agonist for which a combination can be administered on a daily or regular basis to achieve desired results is 0.001-100 mg/kg body mass. Other preferred dosage range is 0.001-30 mg/kg body mass. Other preferred dosage range is 0.001-10 mg/kg body mass. Other preferred dosage range is 0.001-3.0 mg/kg body mass. Other preferred dosage range is 0.001-1.0 mg/kg body mass. Other preferred dosage range is 0.001-0.3 mg/kg body mass. Other preferred dosage range is 0.001-0.1 mg/kg body mass. Other preferred dosage range is 0.001-0.03 mg/kg body mass. Other preferred dosage range is 0.001-0.01 mg/kg body mass. Of course, these daily dosages can be delivered or administered in small amounts periodically during the course of a day. It is noted that these dosage ranges are only preferred ranges and are not meant to be limiting to the invention.

It is expressly contemplated that a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor can be administered on a daily or regular basis to achieve an increased level of GIP in an individual. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual that is 110% to 1000%, 110% to 900%, 110% to 800%, 110% to 700%, 110% to 600%, 110% to 500%, 110% to 400%, 110% to 300%, 110% to 200%, or 110% to 150% a normal blood level of GIP (e.g., a normal pre-meal plasma GIP level or a plasma GIP level between the normal pre-meal and post-meal

plasma GIP levels) in an individual or the blood level of GIP in the individual prior to treatment. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual that is 150% to 1000%, 150% to 900%, 150% to 800%, 150% to 700%, 150% to 600%, 150% to 500%, 150% to 400%, 150% to 300%, or 150% to 200% a normal blood level of GIP (e.g., a normal pre-meal plasma GIP level or a plasma GIP level between the normal pre-meal and post-meal plasma GIP levels) in an individual or the blood level of GIP in the individual prior to treatment. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual that is 200% to 1000%, 200% to 900%, 200% to 800%, 200% to 700%, 200% to 600%, 200% to 500%, 200% to 400%, or 200% to 300% a normal blood level of GIP (e.g., a normal pre-meal plasma GIP level or a plasma GIP level between the normal pre-meal and post-meal plasma GIP levels) in an individual or the blood level of GIP in the individual prior to treatment. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual that is 250% to 1000%, 250% to 900%, 250% to 800%, 250% to 700%, 250% to 600%, 250% to 500%, 250% to 400%, or 250% to 300% a normal blood level of GIP (e.g., a normal pre-meal plasma GIP level or a plasma GIP level between the normal pre-meal and post-meal plasma GIP levels) in an individual or the blood level of GIP in the individual prior to treatment. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual that is 300% to 1000%, 300% to 900%, 300% to 800%, 300% to 700%, 300% to 600%, 300% to 500%, or 300% to 400% a normal blood level of GIP (e.g., a normal pre-meal plasma GIP level or a plasma GIP level between the normal pre-meal and post-meal plasma GIP levels) in an individual or the blood level of GIP in the individual prior to treatment. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual that is 400% to 1000%, 400% to 900%, 400% to 800%, 400% to 700%, 400% to 600%, or 400% to 500% a normal blood level of GIP (e.g., a normal pre-meal plasma GIP level or a plasma GIP level between the normal pre-meal and post-meal plasma GIP levels) in an individual or the blood level of GIP in the individual prior to treatment. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual that is 500% to 1000%, 500% to 900%, 500% to 800%, 500% to 700%, or 500% to 600% a normal blood level of GIP (e.g., a normal pre-meal plasma GIP level or a plasma GIP level between the normal pre-meal and post-meal plasma GIP levels) in an individual or the blood level of GIP in the individual prior to treatment. In certain embodiments, the

blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of total GIP. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of bioactive (active) GIP. It is noted that these ranges of increased blood level of GIP are exemplary ranges and are not meant to be limiting to the invention.

It is expressly contemplated that a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor can be administered on a daily or regular basis to achieve an increased level of GIP in an individual. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased blood (e.g., plasma or serum) level of GIP in an individual. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 100 pg/ml to 2000 pg/ml, 100 pg/ml to 1900 pg/ml, 100 pg/ml to 1800 pg/ml, 100 pg/ml to 1700 pg/ml, 100 pg/ml to 1600 pg/ml, 100 pg/ml to 1500 pg/ml, 100 pg/ml to 1400 pg/ml, 100 pg/ml to 1300 pg/ml, 100 pg/ml to 1200 pg/ml, 100 pg/ml to 1100 pg/ml, 100 pg/ml to 1000 pg/ml, 100 pg/ml to 900 pg/ml, 100 pg/ml to 800 pg/ml, 100 pg/ml to 700 pg/ml, 100 pg/ml to 600 pg/ml, 100 pg/ml to 500 pg/ml, 100 pg/ml to 400 pg/ml, 100 pg/ml to 300 pg/ml, or 100 pg/ml to 200 pg/ml. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 200 pg/ml to 2000 pg/ml, 200 pg/ml to 1900 pg/ml, 200 pg/ml to 1800 pg/ml, 200 pg/ml to 1700 pg/ml, 200 pg/ml to 1600 pg/ml, 200 pg/ml to 1500 pg/ml, 200 pg/ml to 1400 pg/ml, 200 pg/ml to 1300 pg/ml, 200 pg/ml to 1200 pg/ml, 200 pg/ml to 1100 pg/ml, 200 pg/ml to 1000 pg/ml, 200 pg/ml to 900 pg/ml, 200 pg/ml to 800 pg/ml, 200 pg/ml to 700 pg/ml, 200 pg/ml to 600 pg/ml, 200 pg/ml to 500 pg/ml, 200 pg/ml to 400 pg/ml, or 200 pg/ml to 300 pg/ml. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 300 pg/ml to 2000 pg/ml, 300 pg/ml to 1900 pg/ml, 300 pg/ml to 1800 pg/ml, 300 pg/ml to 1700 pg/ml, 300 pg/ml to 1600 pg/ml, 300 pg/ml to 1500 pg/ml, 300 pg/ml to 1400 pg/ml, 300 pg/ml to 1300 pg/ml, 300 pg/ml to 1200 pg/ml, 300 pg/ml to 1100 pg/ml, 300 pg/ml to 1000 pg/ml, 300 pg/ml to 900 pg/ml, 300 pg/ml to 800 pg/ml, 300 pg/ml to 700 pg/ml, 300 pg/ml to 600 pg/ml, 300 pg/ml to 500 pg/ml, or 300 pg/ml to 400 pg/ml. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 400 pg/ml to 2000 pg/ml, 400 pg/ml to 1900 pg/ml, 400 pg/ml to 1800 pg/ml, 400 pg/ml to 1700 pg/ml, 400 pg/ml to 1600 pg/ml, 400 pg/ml to 1500 pg/ml, 400 pg/ml to 1400 pg/ml, 400 pg/ml to 1300 pg/ml, 400 pg/ml to 1200 pg/ml, 400 pg/ml to 1100 pg/ml, 400 pg/ml to 1000 pg/ml, 400 pg/ml to 900 pg/ml, 400 pg/ml to 800 pg/ml, 400 pg/ml to 700 pg/ml, 400 pg/ml to 600 pg/ml, or 400 pg/ml to 500 pg/ml. In certain

embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 500 pg/ml to 2000 pg/ml, 500 pg/ml to 1900 pg/ml, 500 pg/ml to 1800 pg/ml, 500 pg/ml to 1700 pg/ml, 500 pg/ml to 1600 pg/ml, 500 pg/ml to 1500 pg/ml, 500 pg/ml to 1400 pg/ml, 500 pg/ml to 1300 pg/ml, 500 pg/ml to 1200 pg/ml, 500 pg/ml to 1100 pg/ml, 500 pg/ml to 1000 pg/ml, 500 pg/ml to 900 pg/ml, 500 pg/ml to 800 pg/ml, 500 pg/ml to 700 pg/ml, or 500 pg/ml to 600 pg/ml. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 600 pg/ml to 2000 pg/ml, 600 pg/ml to 1900 pg/ml, 600 pg/ml to 1800 pg/ml, 600 pg/ml to 1700 pg/ml, 600 pg/ml to 1600 pg/ml, 600 pg/ml to 1500 pg/ml, 600 pg/ml to 1400 pg/ml, 600 pg/ml to 1300 pg/ml, 600 pg/ml to 1200 pg/ml, 600 pg/ml to 1100 pg/ml, 600 pg/ml to 1000 pg/ml, 600 pg/ml to 900 pg/ml, 600 pg/ml to 800 pg/ml, or 600 pg/ml to 700 pg/ml. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 700 pg/ml to 2000 pg/ml, 700 pg/ml to 1900 pg/ml, 700 pg/ml to 1800 pg/ml, 700 pg/ml to 1700 pg/ml, 700 pg/ml to 1600 pg/ml, 700 pg/ml to 1500 pg/ml, 700 pg/ml to 1400 pg/ml, 700 pg/ml to 1300 pg/ml, 700 pg/ml to 1200 pg/ml, 700 pg/ml to 1100 pg/ml, 700 pg/ml to 1000 pg/ml, 700 pg/ml to 900 pg/ml, or 700 pg/ml to 800 pg/ml. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 800 pg/ml to 2000 pg/ml, 800 pg/ml to 1900 pg/ml, 800 pg/ml to 1800 pg/ml, 800 pg/ml to 1700 pg/ml, 800 pg/ml to 1600 pg/ml, 800 pg/ml to 1500 pg/ml, 800 pg/ml to 1400 pg/ml, 800 pg/ml to 1300 pg/ml, 800 pg/ml to 1200 pg/ml, 800 pg/ml to 1100 pg/ml, 800 pg/ml to 1000 pg/ml, or 800 pg/ml to 900 pg/ml. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 900 pg/ml to 2000 pg/ml, 900 pg/ml to 1900 pg/ml, 900 pg/ml to 1800 pg/ml, 900 pg/ml to 1700 pg/ml, 900 pg/ml to 1600 pg/ml, 900 pg/ml to 1500 pg/ml, 900 pg/ml to 1400 pg/ml, 900 pg/ml to 1300 pg/ml, 900 pg/ml to 1200 pg/ml, 900 pg/ml to 1100 pg/ml, or 900 pg/ml to 1000 pg/ml. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of total GIP. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of bioactive (active) GIP. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve a blood (e.g., plasma or serum) level of GIP in an individual within a concentration range that is 1000 pg/ml to 2000 pg/ml, 1000 pg/ml to 1900 pg/ml, 1000 pg/ml to 1800 pg/ml, 1000 pg/ml to 1700 pg/ml, 1000 pg/ml to 1600 pg/ml, 1000 pg/ml to 1500 pg/ml, 1000 pg/ml to 1400 pg/ml, 1000 pg/ml to 1300

pg/ml, 1000 pg/ml to 1200 pg/ml, or 1000 pg/ml to 1100 pg/ml. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of total GIP. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of bioactive (active) GIP. It is noted that these ranges of blood GIP concentration are exemplary ranges and are not meant to be limiting to the invention.

In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered on a daily or regular basis to achieve an increased level of GIP in an individual in a manner that does not lead to down-regulation or to substantial down-regulation of the GIP receptor (decreased levels of GIP receptor protein) in bone (e.g., in femur) (e.g., in osteoblasts). In certain embodiments, the level of GIP receptor protein in bone is decreased by less than about 90%, less than about 80%, less than about 70%, less than about 60%, less than about 50%, less than about 40%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 5%, or less than about 2.5%. In certain embodiments, the level of GIP receptor protein in bone is decreased by less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 5%, or less than about 2.5%. In certain embodiments, the level of GIP receptor protein in bone is decreased by less than about 10%, less than about 5%, or less than about 2.5%. In certain embodiments, the level of GIP receptor protein in bone is not decreased. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of total GIP. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of bioactive (active) GIP. Suitable animals models (e.g., mouse, rat) for assessing an effect of a GIP level on down-regulation of the GIP receptor in bone are known in the art. Methods for determining down-regulation of the GIP receptor in bone are known to the skilled artisan and include, e.g., Western blot using an antibody to the GIP receptor. *See*, e.g., Xie et al, Bone, 2007.

In certain embodiments, the GPR119 agonist is a GPR119 partial agonist.

In certain embodiments, the GPR119 agonist is a nonendogenous GPR119 agonist.

In certain embodiments, administration of a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is oral.

In certain embodiments related to a combination of a GPR119 agonist and a DPP-IV inhibitor, the GPR119 agonist and the DPP-IV inhibitor are administered in separate dosage forms or in a single dosage form.

In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered in a manner that achieves elevation of GIP in an individual in a pulsatile or episodic fashion. Pulsatile or episodic elevation of GIP shall mean that blood (e.g., plasma or serum) levels of GIP rise from a baseline level to a peak level and return to the baseline level at least one time per day. In certain embodiments, the baseline level of plasma GIP is approximately a normal pre-meal plasma GIP level. In certain embodiments, the baseline level of plasma GIP is

between the normal pre-meal and post-meal plasma GIP levels. The skilled artisan would be aware of how to effect pulsatile or episodic elevation of GIP in an individual. In certain embodiments, pulsatile or episodic elevation is achieved by administering a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor in a manner such that an effect for elevating GIP resulting from the preceding dose completely dissipates before a subsequent dose is administered. In certain embodiments, pulsatile or episodic elevation of GIP is achieved by administering a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor when plasma glucose levels rise (e.g., after ingestion of a meal). In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of total GIP. In certain embodiments, the blood (e.g., plasma or serum) level of GIP is a blood (e.g., plasma or serum) level of bioactive (active) GIP.

It is expressly contemplated that the dosage interval can relate to the time at which a meal is ingested. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered before, during or after a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered before a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 120 minutes or less prior to a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 90 minutes or less prior to a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 60 minutes or less prior to a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 30 minutes or less prior to a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 15 minutes or less prior to a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered during a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered after a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 120 minutes or less after a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 90 minutes or less after a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 60 minutes or less after a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 30 minutes or less after a meal. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered 15 minutes or less after a meal. It is noted that these time intervals are exemplary time intervals and are not meant to be limiting to the invention. In certain embodiments, administration is oral. In certain embodiments related to a combination of a GPR119 agonist and a DPP-IV inhibitor, the GPR119 agonist and the DPP-IV inhibitor are administered in separate dosage forms or in a single dosage form. In certain embodiments, the meal is a daily meal

such as breakfast, lunch, dinner and the like. In certain embodiments, the meal is a regularly scheduled daily meal such as breakfast, lunch, dinner and the like. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered before, during or after one or more daily meals such as breakfast, lunch, dinner and the like. In certain embodiments, a GPR119 agonist or a combination of a GPR119 agonist and a DPP-IV inhibitor is administered before, during or after one or more regularly scheduled daily meals such as breakfast, lunch, dinner and the like.

The term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids. Salts derived from inorganic bases include aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous, potassium, sodium, zinc, and the like. In certain embodiments, salts derived from inorganic bases include the ammonium, calcium, magnesium, potassium, and sodium salts. Salts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, and basic ion exchange resins, such as arginine, betaine, caffeine, choline, N,N'-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethyl-morpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine,, tromethamine, and the like.

When the compound of the present invention is basic, salts may be prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid, and the like. In certain embodiments, such acids include citric, hydrobromic, hydrochloric, maleic, phosphoric, sulfuric, fumaric, and tartaric acids.

Dosage amount and interval may be adjusted individually to provide plasma levels of a GPR119 agonist according to the present invention and/or of a DPP-IV inhibitor according to the present invention which achieve an intended therapeutic effect. It is expressly contemplated, e.g., that the dosage interval of a GPR119 agonist either alone or in combination with a DPP-IV inhibitor can be adjusted to coincide with meals taken by the individual, such as at the time of one or more regular meals (e.g., at breakfast and/or at lunch and/or at dinner, and the like). Dosage intervals can also be determined using the value for a selected range of GPR119 agonist concentration or the value for a selected range of DPP-IV inhibitor concentration so as to achieve the intended therapeutic effect. A GPR119 agonist and/or a DPP-IV inhibitor should be administered using a regimen that maintains

plasma levels within the selected range of GPR119 agonist concentration and/or DPP-IV inhibitor concentration, respectively, for 10-90% of the time, in particular embodiment between 30-99% of the time, and in further particular embodiment between 50-90% of the time. In cases of local administration or selective uptake, the range of GPR119 agonist concentration and/or the range of DPP-IV inhibitor concentration providing the intended therapeutic effect may not be related to plasma concentration.

The amount of composition admininistered will, of course, be dependent on the individual being treated, on the individual's weight, the severity of the affliction, the manner of administration, and the judgement of the prescribing physician.

In one aspect, the present invention accordingly features a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention accordingly features a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in the individual. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect,

the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, wherein the effect is a synergistic effect. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, wherein the effect is a synergistic effect, and wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual, wherein the effect given by the combination of the amount of a GPR119 agonist and the amount of the DPP-IV inhibitor is greater than the effect given by the amount of the GPR119 agonist alone and the effect given by the amount of the DPP-IV inhibitor alone. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist is administered in an amount sufficient to give an effect in increasing a GIP level in the individual. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising

administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in increasing a GIP level in the individual. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in increasing a GIP level in the individual, and wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in increasing a GIP level in the individual. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass, such as osteoporosis, or of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in increasing a GIP level in the individual, and wherein the effect is a synergistic effect. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in increasing a GIP level in the individual, wherein the effect is a synergistic effect, and wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in increasing a GIP level in the individual. In certain embodiments, the composition is a pharmaceutical composition.

In one aspect, the present invention relates to a method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a

therapeutically effective amount of a composition comprising or consisting essentially of an amount of a GPR119 agonist according to the present invention and an amount of a DPP-IV inhibitor according to the present invention. In a related aspect, the present invention features said method wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to give an effect in increasing a GIP level in the individual, wherein the effect given by the combination of the amount of the GPR119 agonist and the amount of the DPP-IV inhibitor is greater than the effect given by the amount of the GPR119 agonist alone and the effect given by the amount of the DPP-IV inhibitor alone. In certain embodiments, the composition is a pharmaceutical composition.

In certain embodiments, the GIP level is a blood or plasma total GIP level. In certain embodiments, the GIP level is a blood or plasma bioactive GIP level.

Therapies of the present invention are useful for increasing bone formation in an individual.

Therapies of the present invention, namely therapies relating to a GPR119 agonist optionally in combination with a DPP-IV inhibitor and including the combination therapy relating to a GPR119 agonist and a DPP-IV inhibitor described above are useful in treating or preventing a condition characterized by low bone mass in an individiual and in increasing bone mass in an individual.

In certain embodiments, the individual receiving a therapy of the present invention, namely a therapy relating to a GPR119 agonist optionally in combination with a DPP-IV inhibitor and including the combination therapy relating to a GPR119 agonist and a DPP-IV inhibitor described above is a human and a participant in a study reviewed by a governmental agency charged with marketing approval for a drug. In certain embodiments, the study is a clinical trial. In certain embodiments, the governmental agency is the Food and Drug Administration of the United States.

Conditions characterized by low bone mass include but are not limited to osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, the condition characterized by low bone mass is osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. Conditions characterized by low bone mass also include but are not limited to long-term complications of osteoporosis such as curvature of the spine, loss of height and prosthetic surgery. It is understood that conditions characterized by low bone mass can be included in embodiments individually or in any combination. In certain embodiments, the condition characterized by low bone mass is primary osteoporosis.

In certain embodiments, the individual in need of increased bone mass has a bone mineral density (BMD) of greater than 1 (T-score < -1), greater than or equal to 1.5 (T-score ≤ -1.5), greater than or equal to 2 (T-score ≤ -2) or greater than or equal to 2.5 (T-score ≤ -2.5) standard deviations below the young adult reference mean. In certain embodiments, the individual in need of increased bone mass is in need of treatment of bone fracture. In certain embodiments, the individual in need of

treatment of a bone fracture has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic bone fracture. In certain embodiments, the individual is in need of treatment for a bone disease. In certain embodiments, the individual in need of treatment for a bone disease has osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, or loss of height. In certain embodiments, the individual in need of treatment for a bone disease has osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. Destructive bone disorders that can be treated according to the invention include but are not limited to osteoporosis, primary osteoporosis, secondary osteoporosis, osteoarthritis, and osteolytic lesions such as those caused by neoplastic disease, radiotherapy, or chemotherapy.

Therapies of the present invention, namely therapies relating to a GPR119 agonist optionally in combination with a DPP-IV inhibitor and including the combination therapy relating to a GPR119 agonist and a DPP-IV inhibitor described above are additionally useful in the treatment of bone fracture. In certain embodiments, the individual in need of treatment of a bone fracture has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic bone fracture.

Therapies of the present invention, namely therapies relating to a GPR119 agonist optionally in combination with a DPP-IV inhibitor and including the combination therapy relating to a GPR119 agonist and a DPP-IV inhibitor described above are additionally useful in the treatment of a bone disease. In certain embodiments, the individual in need of treatment for a bone disease has osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, or loss of height. In certain embodiments, the individual in need of treatment for a bone disease has osteoporosis. In certain embodiments, osteoporosis is primary osteoporosis. In certain embodiments, osteoporosis is secondary osteoporosis. Destructive bone disorders that can be treated according to the invention include but are not limited to osteoporosis, primary osteoporosis, secondary osteoporosis, osteoarthritis, and osteolytic lesions such as those caused by neoplastic disease, radiotherapy, or chemotherapy.

Therapies of the present invention, namely therapies relating to a GPR119 agonist optionally in combination with a DPP-IV inhibitor and including the combination therapy relating to a GPR119 agonist and a DPP-IV inhibitor described above are additionally useful in enhancing bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhancing long bone extension, enhancing prosthetic ingrowth or increasing bone synostosis in an individual.

In certain embodiments, the individual is a vertebrate. In certain embodiments, the individual that is a vertebrate is a fish, an amphibian, a reptile, a bird or a mammal. In certain embodiments, the individual or vertebrate is a mammal. In certain embodiments, the individual or vertebrate that is a

mammal is a mouse, a rat, a hamster, a rabbit, a pig, a dog, a cat, a horse, a cow, a sheep, a goat, a non-human mammal, a non-human primate or a human. In certain embodiments, the individual is a human. In certain embodiments, the human is a post-menopausal woman or a man over the age of 50.

Kits

Also provided by the subject invention are kits for practicing the subject methods, as described above.

In certain embodiments, the kits at least include a composition comprising a GPR119 agonist and instructions for using the components of the kit to practice the subject methods, e.g., methods of treating or preventing a condition characterized by low bone mass, such as osteoporosis, methods of increasing bone mass in an individual, etc. In certain embodiments, the GPR119 agonist is in dosage form. In certain embodiments, the composition is a pharmaceutical composition.

In certain embodiments, the kits at least include a composition comprising a GPR119 agonist and a composition comprising a DPP-IV inhibitor and instructions for using the components of the kit to practice the subject methods, e.g., methods of treating or preventing a condition characterized by low bone mass, such as osteoporosis, methods of increasing bone mass in an individual, etc. In certain embodiments, the GPR119 agonist and/or the DPP-IV is in dosage form. In certain embodiments, the composition comprising a GPR119 agonist and the composition comprising a DPP-IV inhibitor are pharmaceutical compositions.

In certain embodiments, the kits at least include a composition comprising a GPR119 agonist in combination with a DPP-IV inhibitor and instructions for using the components of the kit to practice the subject methods, e.g., methods of treating or preventing a condition characterized by low bone mass, such as osteoporosis, methods of increasing bone mass in an individual, etc. In certain embodiments, the GPR119 agonist in combination with the DPP-IV inhibitor is in dosage form. In certain embodiments, the composition is a pharmaceutical composition.

It is expressly contemplated that the instructions may at least include (as separate or combined instructions) one or both of dosage information and educational information for using the components of the kit to practice the subject methods. Educational material may relate to safer practice of the subject methods, greater compliance with practice of the subject methods, etc. The instructions for practicing the subject methods are generally recorded on a suitable recording medium. For example, the instructions may be printed on a substrate, such as paper or plastic, etc. As such, the instructions may be present in the kits as a package insert, in the labeling of the container of the kit or components thereof (i.e., associated with the packaging or subpackaging) etc. In other embodiments, the instructions are present as an electronic storage data file present on a suitable computer readable storage medium, e.g., CD-ROM, diskette, etc. In yet other embodiments, the actual instructions are not present in the kit, but means for obtaining the instructions from a remote source, e.g., via the internet, are provided. An example of this embodiment is a kit that includes a web address where the

instructions can be viewed and/or from which the instructions can be downloaded. As with the instructions, this means for obtaining the instructions is recorded on a suitable substrate.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, practice the present invention to its fullest extent. The foregoing detailed description is given for clearness of understanding only, and no unnecessary limitation should be understood therefrom, as modifications within the scope of the invention may become apparent to those skilled in the art.

This application claims the benefit of priority from the following provisional applications, filed via U.S. Express mail with the United States Patent and Trademark Office on the indicated dates: U.S. Provisional Number 60/791,613, filed April 11, 2006; U.S. Provisional Number 60/834,737, filed July 31, 2006; and U.S. Provisional Number 60/851,244, filed October 12, 2006; the disclosures of each of which are incorporated herein by reference in their entireties.

Throughout this application, various publications, patents and patent applications are cited. The disclosures of these publications, patents and patent applications referenced in this application are herein incorporated by reference in their entirety into the present disclosure. Citation herein by Applicant of a publication, patent, or patent application is not an admission by Applicant of said publication, patent, or patent application as prior art.

EXAMPLES

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, practice the present invention to its fullest extent. The following detailed examples are to be construed as merely illustrative, and not limitations of the preceding disclosure in any way whatsoever. Those skilled in the art will promptly recognize appropriate variations from the procedures.

EXAMPLE 1: PHARMACODYNAMIC ANALYSIS OF AN EFFECT OF ADMINISTRATION OF GPR119 AGONIST ON BLOOD GIP LEVEL IN WILD-TYPE MICE

A. C57blk/6 male mice were fasted for 18 hours, and randomly assigned into fourteen groups with n=6 for each group. Mice were administered per orally with vehicle (PET; 80% PEG400, 10% ethanol, 10% Tween80) or with a GPR119 agonist in accordance with the present invention (**Compound 1Z**; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine) at 20 mg/kg, as indicated in ***Figure 1A***. Thirty minutes after treatment, a glucose bolus at 3g/kg were delivered per orally, and plasma were collected at 0 (no glucose bolus), 2, 5, 10, 20, 40 and 60 minutes after glucose bolus. Plasma GIP levels were determined

by using a rodent GIP ELISA kit purchased from Linco Research Laboratory [Rat/Mouse Gastric Inhibitory Polypeptide (Total) ELISA Catalog # EZRMGIP-55K], following instructions provided by the supplier. From the results shown in ***Figure 1A***, it is apparent that administration of the GPR119 agonist increased both a glucose-dependent and a glucose-independent level of GIP in the blood of the mice. **Compound 1Z** stimulated plasma total GIP in the mice. **Compound 1Z** is identical to a compound disclosed in International Patent Application No. PCT/US2004/001267 (published as WO 2004/065380).

B. C57blk/6 male mice were fasted for 18 hours, and randomly assigned into fourteen groups with n=6 for each group. Mice were administered per orally with vehicle (20% hydroxypropyl-β-cyclodextrin (HPCD)) or with a GPR119 agonist in accordance with the present invention (**Compound 3Z**) at 10 mg/kg, as indicated in ***Figure 1B***. Thirty minutes after treatment, a glucose bolus at 3g/kg were delivered per orally, and plasma were collected at 0 (no glucose bolus), 5, 10, 20, 60 and 120 minutes after glucose bolus. Plasma GIP levels were determined by using a rodent GIP ELISA kit purchased from Linco Research Laboratory [Rat/Mouse Gastric Inhibitory Polypeptide (Total) ELISA Catalog # EZRMGIP-55K], following instructions provided by the supplier. Statistical analysis was performed using Excel program. Mean values of GIP concentration were calculated based on results with six mice in each group and shown as mean ±SEM. From the results shown in ***Figure 1B***, it is apparent that administration of the GPR119 agonist increased both a glucose-dependent and a glucose-independent level of GIP in the blood of the mice. **Compound 3Z** stimulated plasma total GIP in the mice. **Compound 3Z** is identical to a compound disclosed in International Patent Application No. PCT/US2004/022327 (published as WO 2005/007647).

C. C57blk/6 male mice were fasted for 18 hours, and randomly assigned into fourteen groups with n=6 for each group. Mice were administered per orally with vehicle (20% hydroxypropyl-β-cyclodextrin (HPCD)) or with a GPR119 agonist in accordance with the present invention (**Compound 3Z**) at 1, 3, or 10 mg/kg. Thirty minutes after treatment, a glucose bolus at 3g/kg was delivered per orally, and plasma were collected at 0 (no glucose bolus) or 5 minutes after glucose bolus. Plasma GIP levels were determined by using a rodent GIP ELISA kit purchased from Linco Research Laboratory [Rat/Mouse Gastric Inhibitory Peptide (Total) ELISA Catalog # EZRMGIP-55K], following instructions provided by the supplier. Statistical analysis was performed using Excel program. Mean values of GIP concentration were calculated based on results with six mice in each group and are shown in ***Figure 1C***. From ***Figure 1C***, it is apparent that the GPR119 agonist (**Compound 3Z**) stimulated plasma total GIP in the mice in a dose-dependent manner. **Compound 3Z** is identical to a compound disclosed in International Patent Application No. PCT/US2004/022327 (published as WO 2005/007647).

EXAMPLE 2: EFFECT OF ADMINISTRATION OF GPR119 AGONIST ON BLOOD GIP LEVEL IN GPR119-DEFICIENT (KNOCKOUT) MICE COMPARED TO WILD-TYPE MICE

A. GPR119-deficient male mice and wild-type littermates were fasted for 18 hours. Mice were administered per orally with vehicle (PET; 80% PEG400, 10% ethanol, 10% Tween80) or with a GPR119 agonist in accordance with the present invention (**Compound 1Z**; (2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine) at 20 mg/kg, as indicated (n=5). Thirty minutes after treatment, blood (100 microliter) was collected via retro orbital vein of the eye (time 0) followed by a glucose bolus at 3g/kg (per orally). Five minutes after delivering glucose, another blood sample (100 microliter) was collected (time 5 minutes). Plasma were collected after centrifugation and GIP levels were determined by using a rodent GIP ELISA kit purchased from Linco Research Laboratory [Rat/Mouse Gastric Inhibitory Polypeptide (Total) ELISA Catalog # EZRMGIP-55K], following instructions provided by the supplier. From the results shown in ***Figure 2A***, it is apparent that functional GPR119 receptor was necessary for the administered GPR119 agonist to increase a glucose-independent level and a glucose-dependent level of GIP in the blood of the mice. **Compound 1Z** stimulated plasma total GIP in the wild-type mice. **Compound 1Z** is identical to a compound disclosed in International Patent Application No. PCT/US2004/001267 (published as WO 2004/065380).

B. GPR119-deficient male mice and wild-type littermates were fasted for 18 hours. Mice were administered per orally with vehicle (40% hydroxypropyl-β-cyclodextrin (HPCD)) or with a GPR119 agonist in accordance with the present invention (**Compound 2Z**) at 30 mg/kg, as indicated (n=5). Thirty minutes after treatment, blood (100 microliter) was collected via retro orbital vein of the eye (time 0) followed by a glucose bolus at 3g/kg (per orally). Five minutes after delivering glucose, another blood sample (100 microliter) was collected (time 5 minutes). Plasma were collected after centrifugation and GIP levels were determined by using a rodent GIP ELISA kit purchased from Linco Research Laboratory [Rat/Mouse Gastric Inhibitory Polypeptide (Total) ELISA Catalog # EZRMGIP-55K], following instructions provided by the supplier. Mean values of GIP concentration were calculated based on results with five mice in each group. From the results shown in ***Figure 2B***, it is apparent that functional GPR119 receptor was necessary for the administered GPR119 agonist to increase a glucose-independent level and a glucose-dependent level of GIP in the blood of the mice. **Compound 2Z** stimulated plasma total GIP in the wild-type mice. **Compound 2Z** is identical to a compound disclosed in International Patent Application No. PCT/US2004/022417 (published as WO 2005/007658).

EXAMPLE 3: EFFECT OF ADMINISTRATION OF GPR119 AGONIST IN COMBINATION WITH DPP-IV INHIBITOR ON BLOOD GIP LEVEL IN WILD-TYPE MICE

An amount of a GPR119 agonist in combination with an amount of a DPP-IV inhibitor in accordance with the present invention can be shown to increase a level of GIP in the blood of an individual using the *in vivo* assay described below.

C57blk/6 male mice are fasted for 18 hours, and randomly assigned into fourteen groups with n=6 for each group. Mice are administered per orally with vehicle (PET; 80% PEG400, 10% ethanol, 10% Tween80) or an amount of a GPR119 agonist in combination with an amount of a DPP-IV inhibitor. The experimental groups are analogous to those of Example 1 above. Each of the combined GPR119 agonist and DPP-IV inhibitor is used at an amount between 0.001 mg/kg body weight and 100 mg/kg body weight. Thirty minutes after treatment, a glucose bolus at 3g/kg is delivered per orally, and plasma is collected at 0 (no glucose bolus), 2, 5, 10, 20, 40 and 60 minutes after glucose bolus. Plasma GIP levels are determined by using a rodent GIP ELISA kit purchased from Linco Research Laboratory [Rat/Mouse Gastric Inhibitory Polypeptide (Total) ELISA Catalog # EZRMGIP-55K], following instructions provided by the supplier.

The assay may in related version include additional experimental groups wherein the mice are injected with the amount of the GPR119 agonist alone and/or additional experimental groups wherein the mice are injected with the amount of the DPP-IV inhibitor alone.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in increasing a blood GIP level in the individual, wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in increasing a blood GIP level in the individual using theforegoing *in vivo* assay.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in increasing a blood GIP level in the individual, wherein the effect is a synergistic effect using the foregoing *in vivo* assay.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in increasing a blood GIP level in the individual, wherein the effect is a synergistic effect, and wherein the amount of the GPR119 agonist alone and the amount of a DPP-IV inhibitor alone are not therapeutically effective in increasing a blood GIP level in the individual using the foregoing *in vivo* assay.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in increasing a blood GIP level in the individual, wherein the effect given by the combination of the GPR119 agonist and the DPP-IV inhibitor is greater than the effect given by the amount of the GPR119 agonist alone and the effect given by the amount of the DPP-IV inhibitor alone using the foregoing *in vivo* assay.

EXAMPLE 4: PHARMACODYNAMIC ANALYSIS OF AN EFFECT OF ADMINISTRATION OF GPR119 AGONIST IN COMBINATION WITH DPP-IV INHIBITOR ON BLOOD GIP LEVEL IN WILD-TYPE MICE

An amount of a GPR119 agonist in combination with an amount of a DPP-IV inhibitor in accordance with the present invention was shown to increase a level of GIP in the blood of an individual using the *in vivo* assay of Example 3, *supra*.

C57blk/6 male mice were fasted for 18 hours, and randomly assigned into twenty-four groups with n=6 for each group. Mice were administered per orally with vehicle (PET; 80% PEG400, 10% ethanol, 10% Tween80), with a DPP-IV inhibitor in accordance with the present invention (AR247810) alone at 1mg/kg, or with a combination of a GPR119 agonist ((2-Fluoro-4-methanesulfonyl-phenyl)-{6-[4-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-5-nitro-pyrimidin-4-yl}-amine) at 10 mg/kg and the DPP-IV inhibitor (AR247810) at 1 mg/kg in accordance with the present invention, as indicated in ***Figure 3***. Thirty minutes after treatment, a glucose bolus at 3g/kg were delivered per orally, and plasma were collected at 0 minute, (no glucose bolus), 5 minutes, 10 minutes, 20 minutes, 40 minutes, 60 minutes, 90 minutes, and 120 minutes after glucose bolus. Plasma total GIP levels were determined by using a rodent GIP ELISA kit purchased from Linco Research Laboratory [Rat/Mouse Gastric Inhibitory Polypeptide (Total) ELISA Catalog # EZRMGIP-55K], following instructions provided by the supplier.

From the results shown in ***Figure 3***, it is apparent that administration of the amount of the GPR119 agonist in combination with the amount of the DPP-IV inhibitor in accordance with the present invention consistently gave an effect in increasing a level of GIP in the blood of in the mice greater than the effect given by the amount of the DPP-IV inhibitor alone.

EXAMPLE 5: EFFECT OF ADMINISTRATION OF GPR119 AGONIST ON BONE MASS IN OVARIECTOMIZED RATS

A GPR119 agonist in accordance with the present invention can be shown to be effective in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual using the *in vivo* ovariectomized (OVX) rat model described below [see, e.g., Bollag et al, Mol Cell Endocrinol (2001) 177:35-41].

Twenty virgin female OVX and 20 virgin non-OVX Sprague-Dawley rats (150-175 g), age 8 weeks, are purchased from Harlan Sprague-Dawley, Inc. (Indianapolis, IN). Animals are fed ad libitum on a normal commercial pellet diet, Teklab Rodent diet (1.46% calcium), with free access to water. The rats are randomly divided into four weight-matched experimental groups and selected to receive per orally vehicle or a GPR119 agonist in accordance with the present invention. Treatment is continued on a daily basis for 6 weeks.

1. **Control.** Ten non-OVX rats are administered per orally vehicle.
2. **Control + Treatment.** Ten non-OVX rats are administered per orally GPR119 agonist.
3. **OVX.** Ten OVX rats are administered per orally vehicle.
4. **OVX + Treatment.** Ten OVX rats are administered per orally GPR119 agonist.

The rats are weighed daily and length measured at baseline and again at 6 weeks. Dual energy X-ray absorptiometry (DXA) using a Hologic QDR 1000/W (Waltham, MA) is performed on all animals prior to initiation of treatment and at 6 weeks, and data is analyzed using the software Rat Whole Body version 5.53. Bone mineral density (BMD) is determined at the spine.

The percent change in vertebral bone density after 6 weeks of treatment is determined. It is shown that administration of a GPR119 agonist attenuates the negative effects of ovariectomy on vertebral bone density. Attenuation of the negative effects of ovariectomy on vertebral bone density is indicative of the treatment having efficacy in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual.

EXAMPLE 6: EFFECT OF ADMINISTRATION OF GPR119 AGONIST IN COMBINATION WITH DPP-IV INHIBITOR ON BONE MASS IN OVARIECTOMIZED RATS

A GPR119 agonist in combination with a DPP-IV inhibitor in accordance with the present invention can be shown to be effective in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual using the *in vivo* ovariectomized (OVX) rat model described below [see, e.g., Bollag et al, Mol Cell Endocrinol (2001) 177:35-41].

Twenty virgin female OVX and 20 virgin non-OVX Sprague-Dawley rats (150-175 g), age 8 weeks, are purchased from Harlan Sprague-Dawley, Inc. (Indianapolis, IN). Animals are fed ad libitum on a normal commercial pellet diet, Teklab Rodent diet (1.46% calcium), with free access to water. The rats are randomly divided into four weight-matched experimental groups and selected to receive per orally vehicle or a GPR119 agonist in combination with a DPP-IV inhibitor in accordance with the present invention. Treatment is continued on a daily basis for 6 weeks.

1. **Control.** Ten non-OVX rats are administered per orally vehicle.
2. **Control + Treatment.** Ten non-OVX rats are administered per orally GPR119 agonist in combination with DPP-IV inhibitor.
3. **OVX.** Ten OVX rats are administered per orally vehicle.
4. **OVX + Treatment.** Ten OVX rats are administered per orally GPR119 agonist in combination with DPP-IV inhibitor.

The rats are weighed daily and length measured at baseline and again at 6 weeks. Dual energy X-ray absorptiometry (DXA) using a Hologic QDR 1000/W (Waltham, MA) is performed on all animals prior to initiation of treatment and at 6 weeks, and data is analyzed using the software Rat Whole Body version 5.53.

The percent change in vertebral bone density after 6 weeks of treatment is determined. It is shown that administration of a GPR119 agonist attenuates the negative effects of ovariectomy on vertebral bone density. Attenuation of the negative effects of ovariectomy on vertebral bone density is indicative of the treatment having efficacy in treating or preventing a condition characterized by low bone mass, such as osteoporosis, and/or in increasing bone mass in an individual.

The assay may in related version include additional experimental groups wherein the mice are injected with the amount of the GPR119 agonist alone and/or additional experimental groups wherein the mice are injected with the amount of the DPP-IV inhibitor alone.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in attenuating the negative effects of ovariectomy on vertebral bone density, wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in attenuating the negative effects of ovariectomy on vertebral bone density using the *in vivo* assay described above.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in attenuating the negative effects of ovariectomy on vertebral bone density, wherein the effect is a synergistic effect using the *in vivo* assay described above.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in attenuating the negative effects of ovariectomy on vertebral bone density, wherein the effect is a synergistic effect, and wherein the amount of the GPR119 agonist alone and the amount of a DPP-IV inhibitor alone are not therapeutically effective in attenuating the negative effects of ovariectomy on vertebral bone density using the *in vivo* assay described above.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in attenuating the negative effects of ovariectomy on vertebral bone density, wherein the effect given by the combination of the GPR119 agonist and the DPP-IV inhibitor is greater than the effect given by the amount of the GPR119 agonist alone and the effect given by the amount of the DPP-IV inhibitor alone using the *in vivo* assay described above.

EXAMPLE 7: EFFECT OF ADMINISTRATION OF GPR119 AGONIST ON BONE FRACTURE HEALING

A GPR119 agonist in accordance with the present invention can be shown to be effective in treatment of bone fracture using the *in vivo* assay described below.

Fracture Technique

Sprague-Dawley rats at 3 months of age are anesthetized with Ketamine. A 1 cm incision is made on the anteromedial aspect of the proximal part of the right tibia or femur. The following describes the tibial surgical technique. The incision is carried through to the bone, and a 1 mm hole is drilled 4 mm proximal to the distal aspect of the tibial tuberosity 2 mm medial to the anterior ridge. Intramedullary nailing is performed with a 0.8 mm stainless steel tube (maximum load 36.3 N, maximum stiffness 61.8 N/mm, tested under the same conditions as the bones). No reaming of the medullary canal is performed. A standardized closed fracture is produced 2 mm above the tibiofibular junction by three-point bending using specially designed adjustable forceps with blunt jaws. To minimize soft tissue damage, care is taken not to displace the fracture. The skin is closed with monofilament nylon sutures. The operation is performed under sterile conditions. Radiographs of all fractures are taken immediately after nailing, and rats with fractures outside the specified diaphyseal area or with displaced nails are excluded. The remaining animals are divided randomly into the following groups with 10-12 animals per each subgroup

per time point for testing the fracture healing. The rats are administered on a daily basis per orally with vehicle or with a GPR119 agonist. The GPR119 agonist is used at an amount between 0.001 mg/kg body weight and 100 mg/kg body weight. Treatment is continued for 10, 20, 40 and 80 days.

At 10, 20, 40 and 80 days, 10-12 rats from each group are anesthetized with Ketamine and sacrificed by exsanguination. Both tibiofibular bones are removed by dissection and all soft tissue is stripped. Bones from 5-6 rats for each group are stored in 70% ethanol for histological analysis, and bones from another 5-6 rats for each group are stored in a buffered Ringer's solution (+4°C, pH 7.4) for radiographs and biomechanical testing which is performed.

Histological Analysis

The methods for histological analysis of fractured bone have been previously published by Mosekilde and Bak [Bone (1993) 14:19-27]. Briefly, the fracture site is sawed 8 mm to each side of the fracture line, embedded undecalcified in methymethacrylate, and cut frontals sections on a Reichert-Jung Polycut microtome in 8 μm thick. Masson-Trichome stained mid-frontal sections (including both tibia and fibula) are used for visualization of the cellular and tissue response to fracture healing with and without treatment. Sirius red stained sections are used to demonstrate the characteristics of the callus structure and to differentiate between woven bone and lamellar bone at the fracture site. The following measurements are performed: (1) fracture gap—measured as the shortest distance between the cortical bone ends in the fracture, (2) callus length and callus diameter, (3) total bone volume area of callus, (4) bony tissue per tissue area inside the callus area, (5) fibrous tissue in the callus, and (6) cartilage area in the callus.

Biomechanical analysis

The methods for biomechanical analysis have been previously published by Bak and Andreassen [Calcif Tissue Int (1989) 45:292-297]. Briefly, radiographs of all fractures are taken prior to the biomechanical test. The mechanical properties of the healing fractures are analyzed by a destructive three- or four-point bending procedure. Maximum load, stiffness, energy at maximum load, deflection at maximum load, and maximum stress are determined.

EXAMPLE 8: EFFECT OF ADMINISTRATION OF GPR119 AGONIST IN COMBINATION WITH DPP-IV INHIBITOR ON BONE FRACTURE HEALING

A GPR119 agonist in combination with a DPP-IV inhibitor in accordance with the present invention can be shown to be effective in treatment of bone fracture using the *in vivo* assay described below.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in treating bone fracture in the individual, wherein the amount of the GPR119 agonist alone and the amount of the DPP-IV inhibitor alone are not therapeutically effective in treating bone fracture in the individual using the *in vivo* assay described below.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in treating bone fracture in the individual, wherein the effect is a synergistic effect using the *in vivo* assay described below.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in treating bone fracture in the individual, wherein the effect is a synergistic effect, and wherein the amount of the GPR119 agonist alone and the amount of a DPP-IV inhibitor alone are not therapeutically effective in treating bone fracture in the individual using the *in vivo* assay described below.

It can be shown that a GPR119 agonist and a DPP-IV inhibitor can be provided in amounts sufficient for the combination to give an effect in treating bone fracture in the individual, wherein the effect given by the combination of the GPR119 agonist and the DPP-IV inhibitor is greater than the effect given by the amount of the GPR119 agonist alone and the effect given by the amount of the DPP-IV inhibitor alone using the *in vivo* assay described below.

Fracture Technique

Sprague-Dawley rats at 3 months of age are anesthetized with Ketamine. A 1 cm incision is made on the anteromedial aspect of the proximal part of the right tibia or femur. The following describes the tibial surgical technique. The incision is carried through to the bone, and a 1 mm hole is drilled 4 mm proximal to the distal aspect of the tibial tuberosity 2 mm medial to the anterior ridge. Intramedullary nailing is performed with a 0.8 mm stainless steel tube (maximum load 36.3 N, maximum stiffness 61.8 N/mm, tested under the same conditions as the bones). No reaming of the medullary canal is performed. A standardized closed fracture is produced 2 mm above the tibiofibular junction by three-point bending using specially designed adjustable forceps with blunt jaws. To minimize soft tissue damage, care is taken not to displace the fracture. The skin is closed with monofilament nylon sutures. The operation is performed under sterile conditions. Radiographs of all fractures are taken immediately after nailing, and rats with fractures outside the specified diaphyseal area or with displaced nails are excluded. The remaining animals are divided randomly into the following groups with 10-12 animals per each subgroup per time point for testing the fracture healing. The rats are administered on a daily basis per orally with vehicle or with a GPR119 agonist in combination with a DPP-IV inhibitor. Each of the combined GPR119 agonist and DPP-IV inhibitor is used at an amount between 0.001 mg/kg body weight and 100 mg/kg body weight. Thirty minutes later, a glucose bolus at 3g/kg is delivered per orally. Treatment is continued for 10, 20, 40 and 80 days.

At 10, 20, 40 and 80 days, 10-12 rats from each group are anesthetized with Ketamine and sacrificed by exsanguination. Both tibiofibular bones are removed by dissection and all soft tissue is stripped. Bones from 5-6 rats for each group are stored in 70% ethanol for histological analysis, and bones from another 5-6 rats for each group are stored in a buffered Ringer's solution (+4°C, pH 7.4) for radiographs and biomechanical testing which is performed.

Histological Analysis

The methods for histological analysis of fractured bone have been previously published by Mosekilde and Bak [Bone (1993) 14:19-27]. Briefly, the fracture site is sawed 8 mm to each side of the fracture line, embedded undecalcified in methymethacrylate, and cut frontals sections on a Reichert-Jung Polycut microtome in 8 μm thick. Masson-Trichome stained mid-frontal sections (including both tibia and fibula) are used for visualization of the cellular and tissue response to fracture healing with and without treatment. Sirius red stained sections are used to demonstrate the characteristics of the callus structure and to differentiate between woven bone and lamellar bone at the fracture site. The following measurements are performed: (1) fracture gap—measured as the shortest distance between the cortical bone ends in the fracture, (2) callus length and callus diameter, (3) total bone volume area of callus, (4) bony tissue per tissue area inside the callus area, (5) fibrous tissue in the callus, and (6) cartilage area in the callus.

Biomechanical analysis

The methods for biomechanical analysis have been previously published by Bak and Andreassen [Calcif Tissue Int (1989) 45:292-297]. Briefly, radiographs of all fractures are taken prior to the biomechanical test. The mechanical properties of the healing fractures are analyzed by a destructive three- or four-point bending procedure. Maximum load, stiffness, energy at maximum load, deflection at maximum load, and maximum stress are determined.

EXAMPLE 9: MELANOPHORE ASSAY FOR GPR119 AGONIST ACTIVITY

Melanophores are maintained in culture as reported by Potenza et al [Pigment Cell Research (1992) 5:372-378] and transfected with an expression vector encoding a GPR119 receptor (*e.g.*, human GPR119, GenBank® Accession No. AAP72125 and alleles thereof) using electroporation. Following electroporation, the transfected cells are plated into 96 well plates for the assay. The cells are then allowed to grow for 48 hours in order to both recover from the electroporation procedure and attain maximal receptor expression levels.

On the assay day, the growth medium on the cells is replaced with serum-free buffer containing 10nM melatonin. The melatonin acts via an endogenous Gi-coupled GPCR in the melanophores to lower intracellular cAMP levels. In response to lowered cAMP levels, the melanophores translocate their pigment to the center of the cell. The net effect of this is a significant decrease in the absorbance reading of the cell monolayer in the well, measured at 600-650nM.

After a 1-hour incubation in melatonin, the cells become completely pigment-aggregated. At this point a baseline absorbance reading is collected. Serial dilutions of test compounds are then added to the plate, and compounds having GPR119 agonist activity produce increases in intracellular cAMP levels. In response to these increased cAMP levels, the melanophores translocate their pigment back into the cell periphery. After one hour, stimulated cells are fully pigment-dispersed. The cell monolayer in the dispersed state absorbs much more light in the 600-650nm range. The measured

increase in absorbance compared to the baseline reading allows one to quantitate the degree of receptor stimulation and plot a dose-response curve.

Materials and methods relating to melanophore assay are found in U.S. Pat. Nos. 5,462,856 and 6,051,386, the disclosure of each of which is herein incorporated by reference in its entirety.

EXAMPLE 10: IN VITRO ASSAY FOR INHIBITION OF DPP-IV ACTIVITY

Compounds can be evaluated for inhibition of DPP-IV activity using, e.g., the *in vitro* fluorescent assay described by Leiting et al (Biochem J (2003) 371:525-532). In this assay, DPP-IV is assayed continuously in 100 mM Hepes buffer (pH 7.5) and 0.1 mg/ml of BSA in a total volume of 100 µl for 30 min at 37°C, and read using a Spectramax Gemini plate reader (Molecular Devices, Sunnyvale, CA). The fluorogenic peptide Gly-Pro-AMC (where AMC stands for 7-amino-4-methylcoumarin; obtained from Bachem, Torrance, CA) is used as DPP-IV substrate. IC_{50} values for compounds being evaluated are obtained at 50 µM Gly-Pro-AMC, the K_m level of Gly-Pro-AMC concentration.

The protease inhibitory activities of DPP-IV inhibitors can be readily determined by methods known to those of ordinary skill in the art since suitable *in vitro* assays for measuring protease activity and the inhibition thereof by test compounds are known.

In other exemplary *in vitro* assay for DPP-IV inhibition, solutions of test compounds in varying concentrations (≤10mM final concentration) are prepared in Dimethyl Sulfoxide (DMSO) and then diluted into assay buffer comprising: 20mM Tris, pH 7.4; 20mM KCl; and 0.1 mg/mL BSA. Human DPP-IV (0.1 nM final concentration) is added to the dilutions and pre-incubated for 10 minutes at ambient temperature before the reaction is initiated with A-P-7-amido-4-trifluoromethylcoumarin (AP-AFC; 10 µM final concentration). The total volume of the reaction mixture is 10-100 µL depending on assay formats used (384 or 96 well plates). The reaction is followed kinetically (excitation λ=400 nm; emission λ=505 nm) for 5-10 minutes or an end-point is measured after 10 minutes. Inhibition constants (IC_{50}) are calculated from the enzyme progress curves using standard mathematical models.

Compounds can also be evaluated for inhibition of DPP-IV activity for a fee by a company that provides the service. By way of example, IC_{50} values for DPP-IV inhibition can be obtained for such compounds through MDS Pharma Services (Catalog # 163910; King of Prussia, PA) in *in vitro* assay using recombinant human DPP-IV.

DPP-IV can be human DPP-IV. DPP-IV can be recombinant human DPP-IV.

EXAMPLE 11: WHOLE CELL ADENYLYL CYCLASE ASSAY FOR GPR119 AGONIST ACTIVITY

Cyclic AMP measurements are done with a Flash Plate™ Adenylyl Cyclase kit (New England Nuclear) according to the supplier's protocol. HEK293 cells are plated in 15-cm tissue culture dish at $12x10^6$ cells per dish in regular growth medium (DMEM/10%FBS). On the next day, 10 µg of either

empty vector DNA or expression plasmid DNA are transfected into cells with lipofectamine (Invitrogen, Carlsbad, CA) according to manufacturer's protocol. After 24 hours in culture, transfected cells are harvested in GIBCO cell dissociation buffer (Cat #13151-014), pelleted by centrifugation for 5 minutes at 1,100 rpm, and carefully re-suspended into an appropriate volume of Assay Buffer (50% 1xPBS and 50% Stimulation Buffer) to give a final cell count at $2x10^6$ cells/ml. Test compounds are prepared in 50µl Assay Buffer at desired assay concentration where indicated, and pipetted into wells of the 96-well Flash Plate. The cell suspension prepared above was then added (50 µl per well). After an incubation time of 60 minutes at room temperature, 100 µl of Detection Mix containing tracer [^{125}I] -cAMP is then added to the wells. Plates are incubated for additional 2 hours followed by counting in a Wallac MicroBeta scintillation counter. Values of cAMP/well are extrapolated from a standard cAMP curve which is included on each assay plate.

An increase in cAMP level in GPR119-transfected HEK293 cells over that in HEK293 cells transfected with empty vector is indicative of a test compound being a compound that stimulates GPR119 receptor functionality.

While the foregoing specification teaches the principles of the present invention, with examples provided for the purpose of illustration, it will be understood that the practice of the invention encompasses all of the usual variations, adaptions, or modifications, as come within the scope of the following claims and its equivalents.

CLAIMS

What is claimed is:

1. A method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist.

2. A method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a pharmaceutically acceptable carrier.

3. The method of claim 1 or claim 2, wherein the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

4. The method of claim 1 or claim 2, wherein the condition characterized by low bone mass is osteoporosis.

5. A method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist.

6. A method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a pharmaceutically acceptable carrier.

7. The method of claim 5 or claim 6, wherein the individual has a bone mineral density (BMD) greater than 1 standard deviations (T-score < -1) below the young adult reference mean.

8. A method of treating bone fracture comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist.

9. A method of treating bone fracture comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a pharmaceutically acceptable carrier.

10. The method of claim 8 or claim 9, wherein the individual has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic bone fracture.

11. A method of treating a bone disease comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist.

12. A method of treating a bone disease comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a pharmaceutically acceptable carrier.

13. The method of claim 11 or claim 12, wherein the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

14. The method of claim 11 or claim 12 wherein the bone disease is osteoporosis.

15. A method of enhancing bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist.

16. A method of enhancing bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a pharmaceutically acceptable carrier.

17. The method of any one of claims 1 to 16, wherein the GPR119 agonist is administered in an amount sufficient to increase a GIP level in the individual.

18. The method of any one of claims 1 to 17, wherein the individual is a human.

19. The method of any one of claims 1 to 18, wherein the GPR119 agonist is an agonist of human GPR119.

20. The method of any one of claims 1 to 19, wherein the GPR119 agonist is a small molecule.

21. The method of any one of claims 1 to 20, wherein the GPR119 agonist has an EC_{50} of less than about 10 μM.

22. Use of a GPR119 agonist for the manufacture of a medicament for the treatment or prevention of a condition characterized by low bone mass in an individual.

23. The use of claim 22, wherein the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

24. The use of claim 22 or claim 23, wherein the condition characterized by low bone mass is osteoporosis.

25. Use of a GPR119 agonist for the manufacture of a medicament for increasing bone mass in an individual.

26. The use of claim 25, wherein the individual has a bone mineral density (BMD) greater than 1 standard deviations (T-score < -1) below the young adult reference mean.

27. Use of a GPR119 agonist for the manufacture of a medicament for treating bone fracture in an individual.

28. The use of claim 27, wherein the bone fracture is traumatic bone fracture, long-term bone fracture, or osteoporotic bone fracture.

29. Use of a GPR119 agonist for the manufacture of a medicament for treating a bone disease in an individual.

30. The use of claim 29, wherein the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

31. The use of claim 29 or claim 30 wherein the bone disease is osteoporosis.

32. Use of a GPR119 agonist for the manufacture of a medicament for enhancing bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis in an individual.

33. The use of any one of claims 22 to 32, wherein the GPR119 agonist is provided in an amount sufficient to increase a GIP level in the individual.

34. The use of any one of claims 22 to 33, wherein the individual is a human.

35. The use of any one of claims 22 to 34, wherein the GPR119 agonist is an agonist of human GPR119.

36. The use of any one of claims 22 to 35, wherein the GPR119 agonist is a small molecule.

37. The use of any one of claims 22 to 36, wherein the GPR119 agonist has an EC_{50} of less than about 10 μM.

38. A method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist and a DPP-IV inhibitor.

39. A method of treating or preventing a condition characterized by low bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a DPP-IV inhibitor and a pharmaceutically acceptable carrier.

40. The method of claim 38 or claim 39, wherein the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis,

osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

41. The method or use of claim 38 or claim 39, wherein the condition characterized by low bone mass is osteoporosis.

42. A method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist and a DPP-IV inhibitor.

43. A method of increasing bone mass comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a DPP-IV inhibitor and a pharmaceutically acceptable carrier.

44. The method of claim 42 or claim 43, wherein the individual has a bone mineral density (BMD) greater than 1 standard deviations (T-score < -1) below the young adult reference mean.

45. A method of treating bone fracture comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist and a DPP-IV inhibitor.

46. A method of treating bone fracture comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a DPP-IV inhibitor and a pharmaceutically acceptable carrier.

47. The method of claim 45 or claim 46, wherein the individual has a traumatic bone fracture, a long-term bone fracture, or an osteoporotic bone fracture.

48. A method of treating a bone disease comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist and a DPP-IV inhibitor.

49. A method of treating a bone disease comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a DPP-IV inhibitor and a pharmaceutically acceptable carrier.

50. The method of claim 48 or claim 49, wherein the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease,

alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

51. The method of claim 48 or claim 49 wherein the bone disease is osteoporosis.

52. A method of enhancing bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis comprising administering to an individual in need thereof a therapeutically effective amount of a GPR119 agonist and a DPP-IV inhibitor.

53. A method of enhancing bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis comprising administering to an individual in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a GPR119 agonist and a DPP-IV inhibitor and a pharmaceutically acceptable carrier.

54. The method of any one of claims 38 to 53, wherein the GPR119 agonist and the DPP-IV inhibitor are administered in amounts sufficient to increase a GIP level in the individual.

55. The method of any one of claims 38 to 54, wherein the individual is a human.

56. The method of any one of claims 38 to 55, wherein the GPR119 agonist is an agonist of human GPR119 and/or the DPP-IV inhibitor is an inhibitor of human DPP-IV.

57. The method of any one of claims 38 to 56, wherein the GPR119 agonist is a small molecule and/or the DPP-IV inhibitor is a small molecule.

58. The method of any one of claims 38 to 57, wherein the GPR119 agonist has an EC_{50} of less than about 10 μM and/or the DPP-IV inhibitor has an IC_{50} of less than about 10 μM.

59. Use of a GPR119 agonist and a DPP-IV inhibitor for the manufacture of a medicament for the treatment or prevention of a condition characterized by low bone mass in an individual.

60. The use of claim 59, wherein the condition characterized by low bone mass is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis,

periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

61. The use of claim 59 or claim 60, wherein the condition characterized by low bone mass is osteoporosis.

62. Use of a GPR119 agonist and a DPP-IV inhibitor for the manufacture of a medicament for increasing bone mass in an individual.

63. The use of claim 62, wherein the individual has a bone mineral density (BMD) greater than 1 standard deviations (T-score < -1) below the young adult reference mean.

64. Use of a GPR119 agonist and a DPP-IV inhibitor for the manufacture of a medicament for treating bone fracture in an individual.

65. The use of claim 64, wherein the bone fracture is traumatic bone fracture, long-term bone fracture, or osteoporotic bone fracture.

66. Use of a GPR119 agonist and a DPP-IV inhibitor for the manufacture of a medicament for treating a bone disease in an individual.

67. The use of claim 66, wherein the bone disease is selected from the group consisting of osteopenia, osteoporosis, rheumatoid arthritis, osteoarthritis, periodontal disease, alveolar bone loss, osteotomy bone loss, childhood idiopathic bone loss, Paget's disease, bone loss due to metastatic cancer, osteolytic lesions, curvature of the spine, and loss of height.

68. The use of claim 66 or claim 67 wherein the bone disease is osteoporosis.

69. Use of a GPR119 agonist and a DPP-IV inhibitor for the manufacture of a medicament for enhancing bone healing following facial reconstruction, maxillary reconstruction, mandibular reconstruction, periodontal disease or tooth extraction, enhanced long bone extension, enhanced prosthetic ingrowth or increased bone synostosis in an individual.

70. The use of any one of claims 59 to 69, wherein the GPR119 agonist and the DPP-IV inhibitor are provided in amounts sufficient to increase a GIP level in the individual.

71. The use of any one of claims 59 to 70, wherein the individual is a human.

72. The use of any one of claims 59 to 71, wherein the GPR119 agonist is an agonist of human GPR119 and/or the DPP-IV inhibitor is an inhibitor of human DPP-IV.

73. The use of any one of claims 59 to 72, wherein the GPR119 agonist is a small molecule and/or the DPP-IV inhibitor is a small molecule.

74. The use of any one of claims 59 to 73, wherein the GPR119 agonist has an EC_{50} of less than about 10 μM and/or the DPP-IV inhibitor has an IC_{50} of less than about 10 μM.