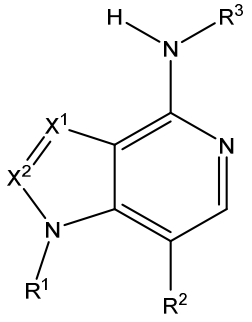
CLAIMS

1. A compound of Formula (I)



(I),

or a tautomer or a stereoisomeric form thereof, or a deuterated form thereof, wherein

X^1 and X^2 are each independently selected from CR^4 and N, with the proviso that one of X^1 or X^2 is N;

R^1 is selected from the group consisting of C_{1-6}alkyl optionally substituted with one or more substituents, each independently selected from the group consisting of halo, -CN, -OC_{1-4}alkyl, OH, $-C(=O)NR^xR^y$, a 5- or 6-membered heteroaryl selected from the group consisting of pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, triazolyl, pyridyl and pyrimidinyl, and C_{3-6}cycloalkyl optionally substituted with one or more independently selected halo substituents, wherein the 5-or 6-membered heteroaryl is optionally substituted with one or two independently selected C_{1-4}alkyl substituents; C_{1-6}alkyl substituted with oxetanyl, C_{1-6}alkyl wherein two geminal hydrogens are replaced by oxetanylidene; tetrahydropyranyl; and a 5- or 6-membered heteroaryl selected from the group consisting of pyrazolyl, imidazolyl, oxazolyl, thiazolyl, triazolyl, pyridyl and pyrimidinyl, each of which may be optionally substituted with or two substituents each independently selected from the group consisting of halo and C_{1-4}alkyl;

with the proviso that a -OC_{1-4}alkyl or -OH substituent, when present, is at least two carbon atoms away from the nitrogen atom of the bicyclic core; wherein

R^x and R^y are each independently selected from the group consisting of hydrogen, C_{1-4}alkyl, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, and C_{3-6}cycloalkyl; or R^x and R^y together with the nitrogen atom to which they are attached form a heterocyclyl ring selected from the group consisting of azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl;

R^2 and R^4 when present, are each independently selected from the group consisting of hydrogen, halo, C_{1-4}alkyl and C_{3-6}cycloalkyl;

R^3 is selected from the group consisting of

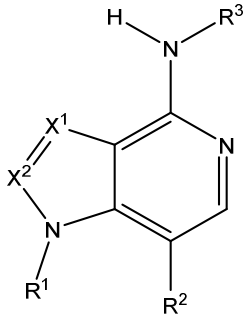
(a) a 5- or 6-membered monocyclic aryl or heteroaryl radical selected from the group consisting of pyrazolyl, phenyl and pyridyl; each of which is substituted with one or more substituents, each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het; and wherein at least one substituent is positioned at the carbon atom ortho- to the NH linker binding R^4 to the bicyclic core; or

(b) a 9- to 10-membered bicyclic heteroaryl radical selected from the group consisting of 1H-indazolyl, 1H-benzo[d]imidazolyl, 1,8-naphthyridinyl, pyrazolo[1,5-a]pyridinyl, imidazo[1,2-a]pyridinyl, imidazo[1,5-a]pyridinyl, imidazo[1,5-b]pyridazinyl, indolizinyl, 1H-indolyl, quinolinyl, isoquinolinyl, and thiazolo[4,5-b]pyridinyl; optionally substituted with one or more substituents each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het;

wherein Het is selected from the group consisting of pyrazolyl, phenyl, pyridyl optionally substituted with one or more substituents, each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, C_{1-4}alkyloxy;

or a pharmaceutically acceptable salt, or a solvate thereof; for use as a medicament.

2. A compound of Formula (I)



(I),

or a tautomer or a stereoisomeric form thereof, or a deuterated form thereof, wherein

X^1 and X^2 are each independently selected from CR^4 and N, with the proviso that one of X^1 or X^2 is N;

R^1 is selected from the group consisting of unsubstituted C_{2-6}alkyl; C_{1-6}alkyl substituted with one or more substituents, each independently selected from the group consisting of halo, -CN, -OC_{1-4}alkyl, OH, -C(=O)NR^xR^y, a 5- or 6-membered heteroaryl selected from the group consisting of pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, triazolyl, pyridyl and pyrimidinyl, and C_{3-6}cycloalkyl optionally substituted with one or more independently selected halo substituents, wherein the 5-or 6-membered heteroaryl is optionally substituted with one or two independently selected C_{1-4}alkyl substituents;

C_{1-6}alkyl substituted with oxetanyl, C_{1-6}alkyl wherein two geminal hydrogens are replaced by oxetanylidene; tetrahydropyranyl; and a 5- or 6-membered heteroaryl selected from the group consisting of pyrazolyl, imidazolyl, oxazolyl, thiazolyl, triazolyl, pyridyl and pyrimidinyl, each of which may be optionally substituted with or two substituents each independently selected from the group consisting of halo and C_{1-4}alkyl;

with the proviso that a -OC_{1-4}alkyl or -OH substituent, when present, is at least two carbon atoms away from the nitrogen atom of the bicyclic core; wherein

R^x and R^y are each independently selected from the group consisting of hydrogen, C_{1-4}alkyl, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, and C_{3-6}cycloalkyl; or R^x and R^y together with the nitrogen atom to which they are attached form a heterocyclyl ring selected from the group consisting of azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl;

R^2 and R^4 when present, are each independently selected from the group consisting of hydrogen, halo, C_{1-4}alkyl and C_{3-6}cycloalkyl;

R^3 is selected from the group consisting of

(a) a 5- or 6-membered monocyclic aryl or heteroaryl radical selected from the group consisting of pyrazolyl, phenyl and pyridyl; each of which is substituted with one or more substituents, each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het; and wherein at least one substituent is positioned at the carbon atom ortho- to the NH linker binding R^4 to the bicyclic core; or

(b) a 9- to 10-membered bicyclic heteroaryl radical selected from the group consisting of 1H-indazolyl, 1H-benzo[d]imidazolyl, 1,8-naphthyridinyl, pyrazolo[1,5-a]pyridinyl, imidazo[1,2-a]pyridinyl, imidazo[1,5-a]pyridinyl, imidazo[1,5-b]pyridazinyl, indolizinyl, 1H-indolyl, quinolinyl, isoquinolinyl, and thiazolo[4,5-b]pyridinyl; optionally substituted with one or more substituents each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het;

wherein Het is selected from the group consisting of pyrazolyl, phenyl, pyridyl optionally substituted with one or more substituents, each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, C_{1-4}alkyloxy;

or a pharmaceutically acceptable salt, or a solvate thereof.

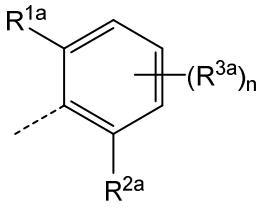
3. The compound according to claim 2, wherein R^3 is selected from the group consisting of

(a) a 5- or 6-membered monocyclic aryl or heteroaryl radical selected from the group consisting of pyrazolyl, phenyl and pyridyl; each of which is substituted with one or more substituents, each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het; and wherein at least one substituent is positioned at the carbon atom ortho- to the NH linker binding R^4 to the bicyclic core; or

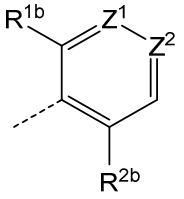
(b) 1H-indazolyl optionally substituted with one or more substituents each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het;

wherein Het is selected from the group consisting of pyrazolyl, phenyl, pyridyl optionally substituted with one or more substituents, each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, and C_{1-4}alkyloxy.

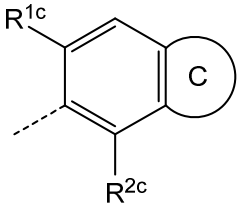
4. The compound according to claim 2 or 3, wherein R^3 is selected from the group consisting of (a), (b), and (c):



(a)



(b)



(c)

wherein R^{1a}, R^{2a}, R^{1b} and R^{2b} are each independently selected from the group consisting of hydrogen, halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het; with the proviso that at least one of R^{1a} or R^{2a}, and at least one of R^{1b} or R^{2b} is not hydrogen;

Z^1 and Z^2 are each independently selected from N, CH or CR^{3b}, with the proviso that at least one of Z^1 or Z^2 is N;

R^{3a} and R^{3b} when present, are each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, -(C=O)C_{1-4}alkyl, and Het; wherein

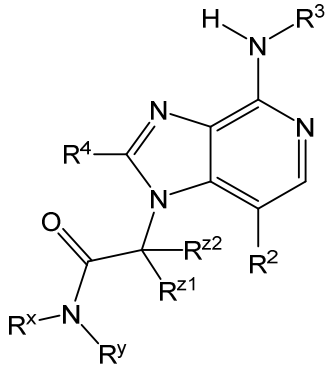
n represents 0, 1 or 2;

Het is selected from the group consisting of pyrazolyl, phenyl, pyridyl optionally substituted with one or more substituents, each independently selected from the group consisting of halo, C_{1-4}alkyl, -CN, and C_{1-4}alkyloxy;

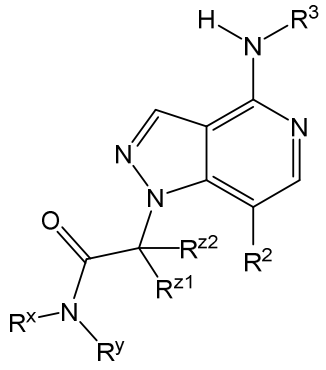
R^{1c} and R^{2c} are each independently selected from the group consisting of hydrogen, halo, C_{1-4}alkyl, -CN, monohaloC_{1-4}alkyl, polyhaloC_{1-4}alkyl, C_{1-4}alkyloxy, monohaloC_{1-4}alkyloxy, polyhaloC_{1-4}alkyloxy, and -(C=O)C_{1-4}alkyl; and

C forms a fused 5-membered heteroaromatic ring selected from the group consisting of pyrazolyl, and imidazolyl, each being optionally substituted with one or more independently selected C_{1-4}alkyl substituents.

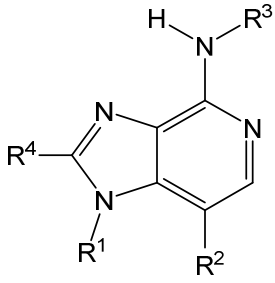
5. The compound according to any one of claims 2 to 4, wherein the compound of Formula (I) has the Formula (I-A), (I-B), (I-C) or (I-D)



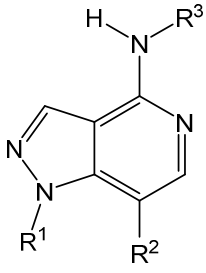
(I-A)



(I-B)



(I-C)



(I-D)

wherein z1 and z2 are each independently selected from hydrogen, deuterium and halogen and the rest of the variables are as defined in any one of claims 2 to 4.

6. A pharmaceutical composition comprising a prophylactically or a therapeutically effective amount of a compound according to any one of claims 2 to 5 and a pharmaceutically acceptable carrier.

7. A process for preparing the pharmaceutical composition according to claim 6, comprising mixing a pharmaceutically acceptable carrier with a prophylactically or a therapeutically effective amount of a compound according to any one of claims 2 to 5.

8. The compound as defined in any one of claims 2 to 5, or the pharmaceutical composition as defined in claim 6, for use as a medicament.

9. The compound for use according to claim 1, in the treatment or prevention of a tauopathy, or an alpha synucleinopathy.

10. The compound as defined in any one of claims 2 to 5, or the pharmaceutical composition as defined in claim 6, for use in the treatment or prevention of a tauopathy, or an alpha synucleinopathy.

11. The compound or the pharmaceutical composition for use according to claim 9 or 10, wherein the tauopathy is selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis and parkinsonism-dementia complex, argyrophilic grain disease, chronic traumatic encephalopathy, corticobasal degeneration, diffuse neurofibrillary tangles with calcification, Down's syndrome, Familial British dementia, Familial Danish dementia, Frontotemporal dementia and parkinsonism linked to chromosome 17 (caused by MAPT mutations), Frontotemporal lobar degeneration (some cases caused by C9ORF72 mutations), Gerstmann-Sträussler-Scheinker disease, Parkinson's disease, Guadeloupean parkinsonism, myotonic dystrophy, neurodegeneration with brain iron accumulation, Niemann-Pick disease, type C, non-Guamanian motor neuron disease with neurofibrillary tangles, Pick's disease, postencephalitic parkinsonism, prion protein cerebral amyloid angiopathy, progressive subcortical gliosis, progressive supranuclear palsy, SLC9A6-related mental retardation, subacute sclerosing panencephalitis, tangle-only dementia, and white matter tauopathy with globular glial inclusions; and the alpha synucleinopathy is selected from the group consisting of Parkinson's disease, dementia due to Parkinson's (or neurocognitive disorder due to Parkinson's disease), dementia with Lewy bodies, multiple system atrophy, and alpha synucleinopathy caused by Gaucher's disease.

12. The compound for use according to claim 1, in the control or reduction of the risk of preclinical Alzheimer's disease, prodromal Alzheimer's disease, or tau-related neurodegeneration as observed in different forms of tauopathies.

13. The compound as defined in any one of claims 2 to 5, or the pharmaceutical composition as defined in claim 6, for use in the control or reduction of the risk of preclinical Alzheimer's disease, prodromal Alzheimer's disease, or tau-related neurodegeneration as observed in different forms of tauopathies.

14. The compound for use as defined in claim 1, in the control or reduction of the risk of prodromal Parkinson's disease.

15. The compound as defined in any one of claims 2 to 5, or the pharmaceutical composition as defined in claim 6, for use in the control or reduction of the risk of prodromal Parkinson's disease.

16. ~~A method of~~Use of a compound as defined in claim 1 in the manufacture of a medicament for preventing or treating a disorder selected from the group consisting of tauopathy or an alpha synucleinopathy, in particular a tauopathy selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis and parkinsonism-dementia complex, argyrophilic grain disease, chronic traumatic encephalopathy, corticobasal degeneration, diffuse neurofibrillary tangles with calcification, Down's syndrome, Familial British dementia, Familial Danish dementia, Frontotemporal dementia and parkinsonism linked to chromosome 17 (caused by MAPT mutations), Frontotemporal lobar degeneration (some cases caused by C9ORF72 mutations), Gerstmann-Sträussler-Scheinker disease, Parkinson's disease, Guadeloupean parkinsonism, myotonic dystrophy, neurodegeneration with brain iron accumulation, Niemann-Pick disease, type C, non-Guamanian motor neuron disease with neurofibrillary tangles, Pick's disease, postencephalitic parkinsonism, prion protein cerebral amyloid angiopathy, progressive subcortical gliosis, progressive supranuclear palsy, SLC9A6-related mental retardation, subacute sclerosing panencephalitis, tangle-only dementia, and white matter tauopathy with globular glial inclusions, or in particular an alpha synucleinopathy selected from the group consisting of Parkinson's disease, dementia due to Parkinson's (or neurocognitive disorder due to Parkinson's disease), dementia with Lewy bodies, multiple system atrophy, and alpha synucleinopathy caused by Gaucher's disease~~, comprising administering to a subject in need thereof, a prophylactically or a therapeutically effective amount of a compound according to any one of claims 2 to 4 or the pharmaceutical composition according to claim 6~~.

17. Use of a compound as defined in any one of claims 2 to 5, or the pharmaceutical composition as defined in claim 6, in the manufacture of a medicament for preventing or treating a disorder selected from the group consisting of tauopathy or an alpha

synucleinopathy, in particular a tauopathy selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis and parkinsonism-dementia complex, argyrophilic grain disease, chronic traumatic encephalopathy, corticobasal degeneration, diffuse neurofibrillary tangles with calcification, Down's syndrome, Familial British dementia, Familial Danish dementia, Frontotemporal dementia and parkinsonism linked to chromosome 17 (caused by MAPT mutations), Frontotemporal lobar degeneration (some cases caused by C9ORF72 mutations), Gerstmann-Sträussler-Scheinker disease, Parkinson's disease, Guadeloupean parkinsonism, myotonic dystrophy, neurodegeneration with brain iron accumulation, Niemann-Pick disease, type C, non-Guamanian motor neuron disease with neurofibrillary tangles, Pick's disease, postencephalitic parkinsonism, prion protein cerebral amyloid angiopathy, progressive subcortical gliosis, progressive supranuclear palsy, SLC9A6-related mental retardation, subacute sclerosing panencephalitis, tangle-only dementia, and white matter tauopathy with globular glial inclusions, or in particular an alpha synucleinopathy selected from the group consisting of Parkinson's disease, dementia due to Parkinson's (or neurocognitive disorder due to Parkinson's disease), dementia with Lewy bodies, multiple system atrophy, and alpha synucleinopathy caused by Gaucher's disease.