

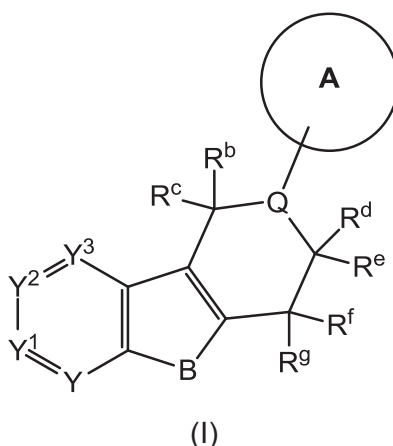
inhibitor, Nilotinib, is tested in clinical trials. Lastly, among the Tau aggregation inhibitors only one, LMTX, is currently in clinical trials (Cummings et al., 2017). Although in recent years, Tau-based treatments have become a point of increasing focus, there is still a big need for additional therapeutic agents that target the pathological Tau conformers that are known or presumed to cause tauopathies.

WO2011/128455 refers to specific compounds which are suitable for treating disorders associated with amyloid proteins or amyloid-like proteins.

WO2010/080253 refers to dipyrindyl-pyrrole derivative compounds which are useful in the treatment of diseases amenable to protein kinase signal transduction inhibition, regulation and/or modulation.

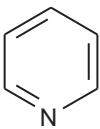
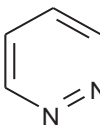
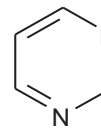
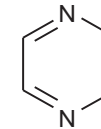
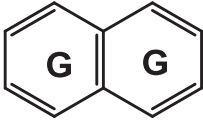
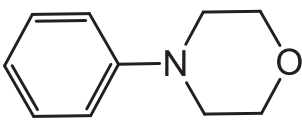
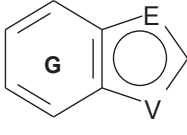
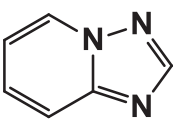
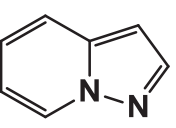
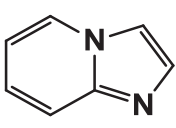
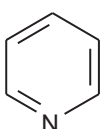
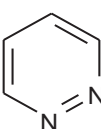
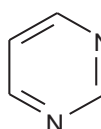
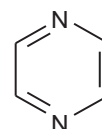
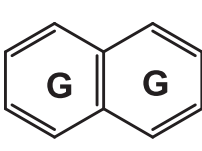
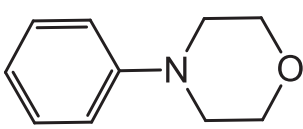
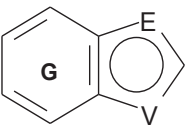
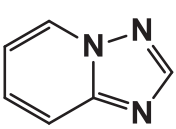
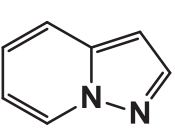
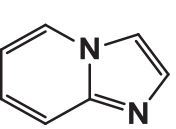
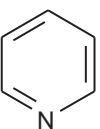
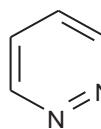
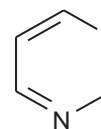
Summary

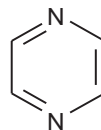
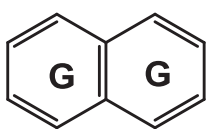
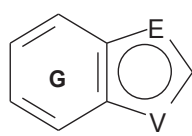
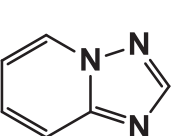
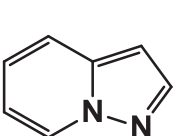
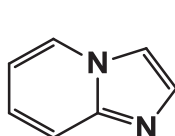
In one aspect, the present disclosure refers to a compound of formula (I):



and all stereoisomers, racemic mixtures, tautomers, pharmaceutically acceptable salts, prodrugs, hydrates, solvates and polymorphs thereof;

wherein

A is selected from the group consisting of , , , , , , , , , and , wherein , , , , , , , , , and , can be attached to Q at any available position, wherein , , ,

 and  is substituted by one or more substituents **R^j**, and wherein , ,  and  can be optionally substituted by one or more substituents **R**;

B is selected from the group consisting of O and NR^a;

E and **V** are independently selected from the group consisting of N, NR⁵, O and S;

G is selected from the group consisting of a benzene ring, a pyrimidine ring and a pyridine ring;

J is selected from the group consisting of O and N-R¹;

Q is selected from the group consisting of N and C–R¹;

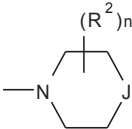
Y is selected from the group consisting of CZ and N, provided that when **Y** is N and **Y**¹, **Y**² and **Y**³ are CZ, **B** is N-alkyl or O;

Y¹ is selected from the group consisting of CZ and N;

Y² is selected from the group consisting of CZ and N;

Y³ is selected from the group consisting of CZ and N;

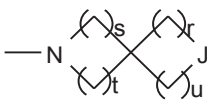
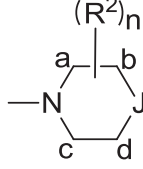
Z is independently selected from the group consisting of H, halogen, O-alkyl, alkyl and CN;

R is independently selected from the group consisting of  and –NR³R⁴;

R^a is selected from the group consisting of H and alkyl;

R^b, **R**^c, **R**^d, **R**^e, **R**^f, and **R**^g are independently selected from the group consisting of H and alkyl, or any two of **R**^b, **R**^c, **R**^d, **R**^e, **R**^f, and **R**^g may be joined to form a 3 to 8-membered ring;

R^j is independently selected from the group consisting of –halogen, –O-alkyl, –CF₃, –CN,

 and , wherein a C₁₋₂ carbon atom-containing bridge can be present between the a carbon atom and the c or d carbon atom or wherein a C₁₋₂ carbon atom-containing bridge can be present between the b carbon atom and the c or d carbon atom;

R¹ is selected from the group consisting of H and alkyl;

R² is independently selected from the group consisting of alkyl, F and =O, wherein the alkyl can be optionally substituted by halogen, –OH or –O–alkyl and wherein if two **R²** are geminal they can be joined to form a 3 to 6-membered ring;

R³ and **R⁴** are independently selected from the group consisting of H and alkyl, wherein the alkyl can be optionally substituted by halogen, –OH or –O–alkyl;

R⁵ is selected from the group consisting of H and alkyl;

n is 0, 1, 2, 3 or 4.

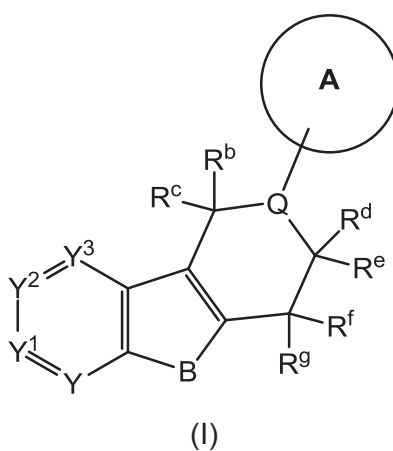
r and **s** are independently 0, 1, 2 or 3; and

t and **u** are independently 1, 2 or 3.

In another aspect, the present disclosure refers to a pharmaceutical composition comprising a compound disclosed herein and optionally a pharmaceutically acceptable carrier or excipient.

In yet another aspect, the present disclosure refers to a compound disclosed herein, for use as a medicament.

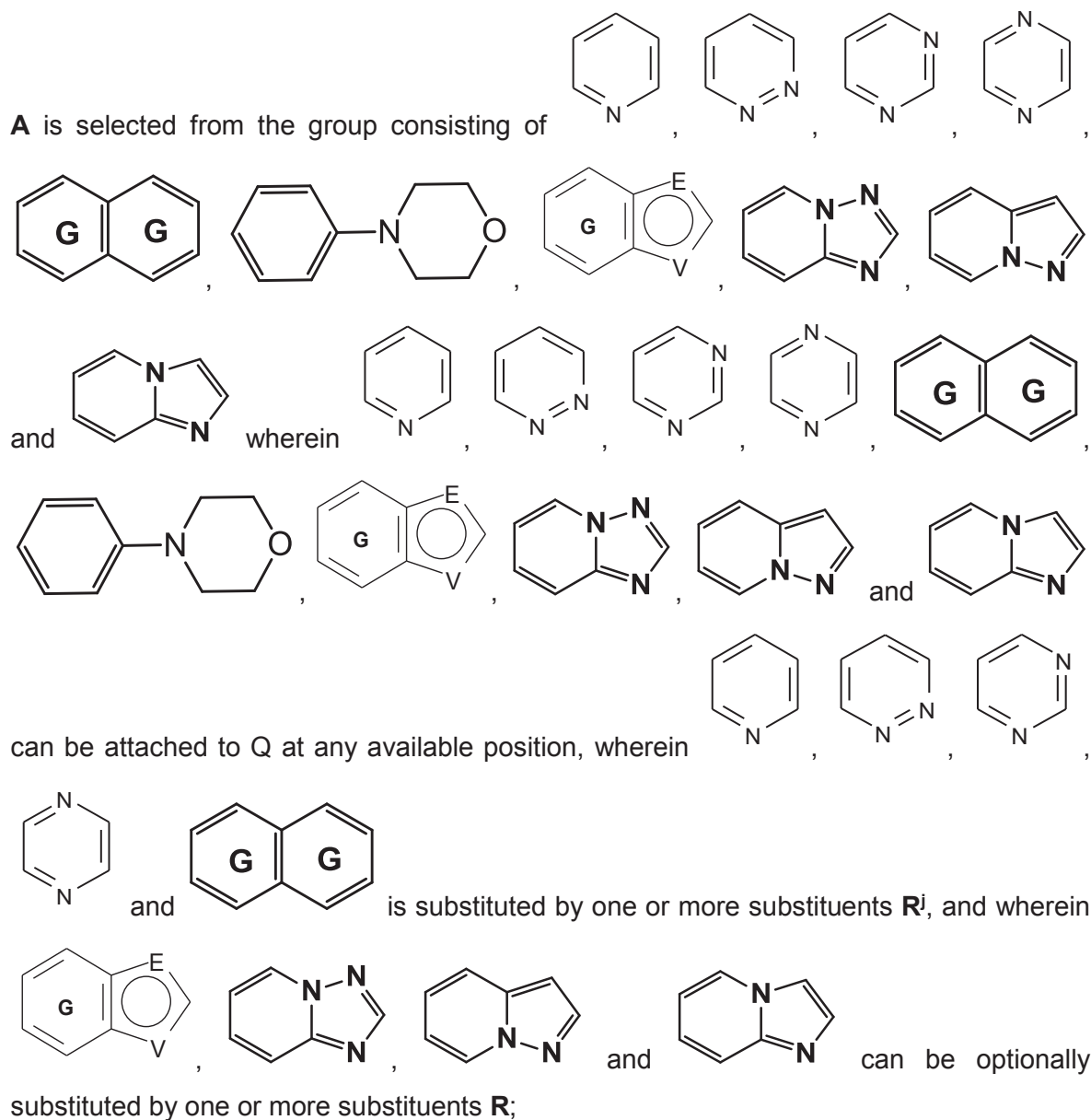
In a further aspect, the present disclosure refers to a compound of formula (I):



and all stereoisomers, racemic mixtures, tautomers, pharmaceutically acceptable salts, prodrugs, hydrates, solvates and polymorphs thereof;

for use in the treatment, alleviation or prevention of a disorder or abnormality associated with Tau protein aggregates,

wherein



B is selected from the group consisting of O and NR^a;

E and **V** are independently selected from the group consisting of N, NR⁵, O and S;

G is selected from the group consisting of a benzene ring, a pyrimidine ring and a pyridine ring;

J is selected from the group consisting of O and N–R¹;

Q is selected from the group consisting of N and C–R¹;

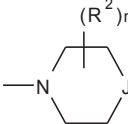
Y is selected from the group consisting of CZ and N;

Y¹ is selected from the group consisting of CZ and N;

Y² is selected from the group consisting of CZ and N;

Y³ is selected from the group consisting of CZ and N;

Z is independently selected from the group consisting of H, halogen, O–alkyl, alkyl and CN;

R is independently selected from the group consisting of  and –NR³R⁴;

R^a is selected from the group consisting of H and alkyl;

R^b, **R**^c, **R**^d, **R**^e, **R**^f, and **R**^g are independently selected from the group consisting of H and alkyl, or any two of **R**^b, **R**^c, **R**^d, **R**^e, **R**^f, and **R**^g may be joined to form a 3 to 8-membered ring;

$\text{—NR}^3\text{R}^4$,  and , wherein a C₁₋₂ carbon atom-containing bridge can be present between the a carbon atom and the c or d carbon atom or wherein a C₁₋₂ carbon atom-containing bridge can be present between the b carbon atom and the c or d carbon atom;

R² is independently selected from the group consisting of alkyl, F and =O, wherein the alkyl can be optionally substituted by halogen, -OH or -O-alkyl and wherein if two **R²** are geminal they can be joined to form a 3 to 6-membered ring;

R⁵ is selected from the group consisting of H and alkyl;

r and **s** are independently 0, 1, 2 or 3; and

In another aspect, the present disclosure refers to a use of a compound disclosed herein, in the manufacture of a medicament for treating, preventing or alleviating a disorder or abnormality associated with Tau protein aggregates.

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In a further aspect, the present disclosure refers to a compound disclosed herein, for use in preventing formation of Tau aggregates and/or for use in inhibiting Tau aggregation.

In another aspect, the present disclosure refers to a compound disclosed herein, for use in interfering intracellularly with Tau aggregates.

In yet another aspect, the present disclosure refers to a compound disclosed herein, for use in reducing Tau misfolding and hyperphosphorylation *in vivo*.

In a further aspect, the present disclosure refers to a compound disclosed herein, for use in reducing neuroinflammatory markers.

In another aspect, the present disclosure refers to a use of a compound disclosed herein, in the manufacture of a medicament for decreasing Tau aggregation

In yet another aspect, the present disclosure refers to a use of a compound disclosed herein, in the manufacture of a medicament for preventing the formation of Tau aggregates and/or for inhibiting Tau aggregation.

In a further aspect, the present disclosure refers to a use of a compound disclosed herein in the manufacture of a medicament for interfering intracellularly with Tau aggregates.

In another aspect, the present disclosure refers to a use of a compound disclosed herein, in the manufacture of a medicament for reducing Tau misfolding and hyperphosphorylation *in vivo*.

In yet another aspect, the present disclosure refers to a use of a compound disclosed herein, in the manufacture of a medicament for reducing neuroinflammatory markers.

In a further aspect, the present disclosure refers to a mixture comprising a compound disclosed herein and at least one further biologically active compound selected from a therapeutic agent different from the compound disclosed herein, wherein the mixture further comprises at least one of a pharmaceutically acceptable carrier, a diluent and an excipient.

In another aspect, the present disclosure refers to a use of the compound disclosed herein as an analytical reference or an *in vitro* screening tool.

It was an object of the present disclosure to provide compounds that can be employed in the treatment, alleviation or prevention of a group of disorders and abnormalities associated with Tau protein aggregates including, but not limited to, NFTs, such as Alzheimer's disease (AD). Furthermore, there exists a need in the art for compounds which can be used as therapeutic agents for (a) decreasing Tau aggregates/NFTs by recognizing aggregated Tau and disaggregating Tau, for example by changing the Tau aggregate molecular conformation, and/or (b) preventing the formation of Tau aggregates, and/or (c) interfering intracellularly with Tau aggregates, and/or (d) reducing Tau misfolding and hyperphosphorylation *in vivo* and/or (f) reducing neuroinflammatory markers. The present inventors have surprisingly found that these objects can be achieved by the compounds of formula (I) as described hereinafter.

The compounds of formula (I) (a) display high capability in decreasing Tau aggregates by recognizing aggregated Tau and disaggregating Tau, for example by changing the Tau aggregate molecular conformation, and/or (b) prevent the formation of Tau aggregates, and/or (c) interfere intracellularly with Tau aggregates, and/or (d) reduce Tau misfolding and hyperphosphorylation *in vivo* and/or (f) reduce neuroinflammatory markers. While not wishing to be bound by theory, it is assumed that the compounds of formula (I) inhibit the Tau aggregation or disaggregate preformed Tau aggregates including when present intracellularly. Due to their

unique design features, these compounds display properties such as appropriate lipophilicity and molecular weight, brain uptake and pharmacokinetics, cell permeability, solubility and metabolic stability, in order to be a successful medicament for the treatment, alleviation or prevention of tauopathies.

The accumulation of Tau NFT lesions has been shown to correlate well with cognitive deficits in AD, both through histopathological analyses as well as through *in vivo* Tau PET imaging. The compounds of this present disclosure can either prevent the formation of Tau aggregates, or disaggregate pre-existing Tau aggregates and can therefore be expected to prevent or reduce the associated cognitive deficits in AD.

Ultrastructural analyses have shown that Tau inclusions are composed of paired helical filaments (PHF) or straight filaments (SF). High resolution structural analyses have shown that these filaments are composed of a core region comprising amino acids 306-378 of Tau which adopt a cross beta / beta-helix structure. The compounds of this present disclosure can recognize aggregated Tau and disaggregate Tau, for example, by changing the Tau aggregate molecular conformation, and can therefore be expected to facilitate Tau clearance.

In addition, it has been shown that Tau is able to both propagate from cell-to-cell and that certain forms of Tau (acting as seeds) are able to induce the structural change of native Tau protein within the healthy cell to undergo misfolding and aggregation. It is considered that aggregated Tau is responsible for the seeding and thus of the Tau pathology spreading. The compounds of this present disclosure can interfere intracellularly with aggregated Tau and can therefore be expected to reduce Tau pathology spreading and finally prevent or reduce the associated cognitive deficits in AD.

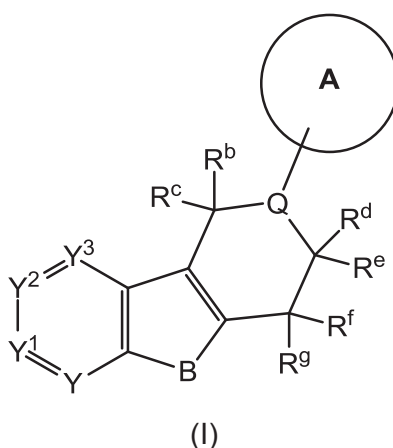
The Tau aggregation cascade initiates with Tau misfolding and hyperphosphorylation. These events are believed to precede the formation of the intracellular Tau neuronal inclusions and therefore the establishment and spreading of the Tau pathology. The compounds of this present disclosure can reduce Tau misfolding and hyperphosphorylation *in vivo* and can therefore be expected to be beneficial in treating, alleviating, or preventing the diseases associated with Tau pathology.

Lastly, the link between Tau pathology and neuroinflammation is now well established. Neuroinflammation is a key event already in early AD stages and is believed to be one of the causes that trigger aggregation of Tau in PHF. Moreover, several tauopathy mouse models showed significant neuroinflammation once the Tau pathology is well established in the brain indicating that Tau pathology can also induce a neuroinflammatory process. These two findings indicate that Tau pathology and neuroinflammation are linked in a positive feedback loop. The compounds of this present disclosure reduce neuroinflammatory markers in the context of Tau pathology.

The present disclosure discloses novel compounds of formula (I) having capabilities to (a) decrease Tau aggregates, recognize aggregated Tau and disaggregate Tau, for example, by changing the Tau aggregate molecular conformation, and/or (b) prevent the formation of Tau aggregates, and/or (c) interfere intracellularly with Tau aggregates, and/or (d) reduce Tau misfolding and hyperphosphorylation *in vivo* and/or (f) reduce neuroinflammatory markers. The present disclosure provides methods for the treatment of disorders and abnormalities associated with Tau protein aggregates including, but not limited to, NFTs, using a compound of formula (I) or a pharmaceutical composition thereof. The present disclosure further provides a pharmaceutical composition comprising a compound of formula (I) and a pharmaceutically acceptable carrier or excipient.

The present disclosure is summarized in the following items:

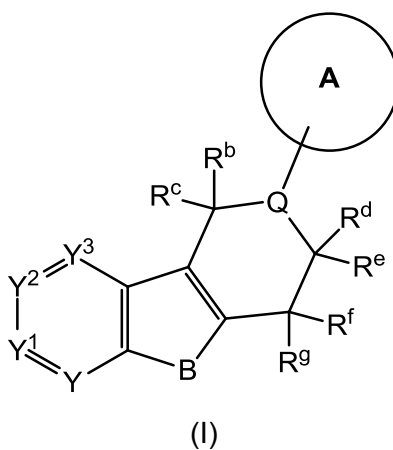
1. A compound of formula (I):



and all stereoisomers, racemic mixtures, tautomers, pharmaceutically acceptable salts, prodrugs, hydrates, solvates and polymorphs thereof;

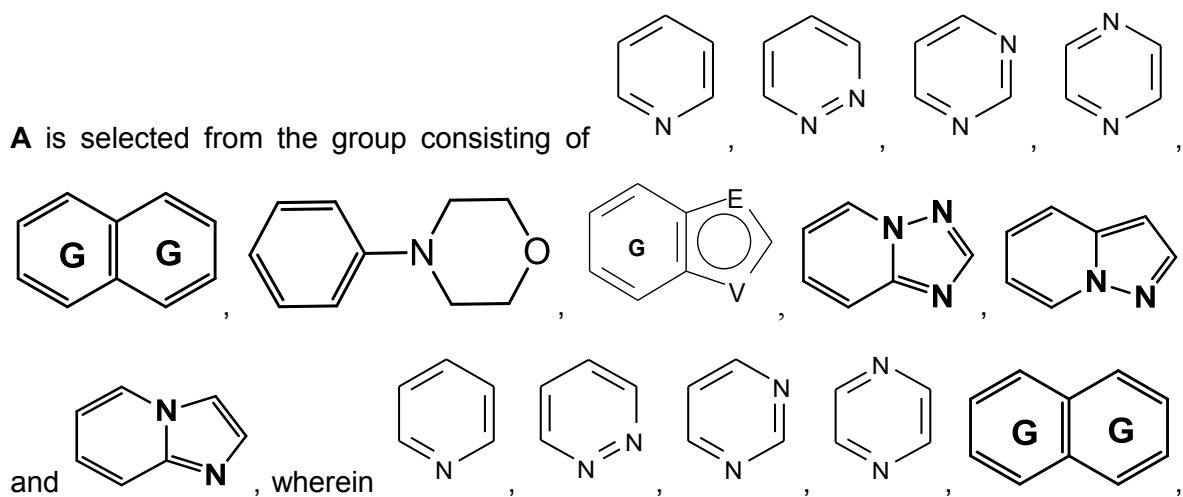
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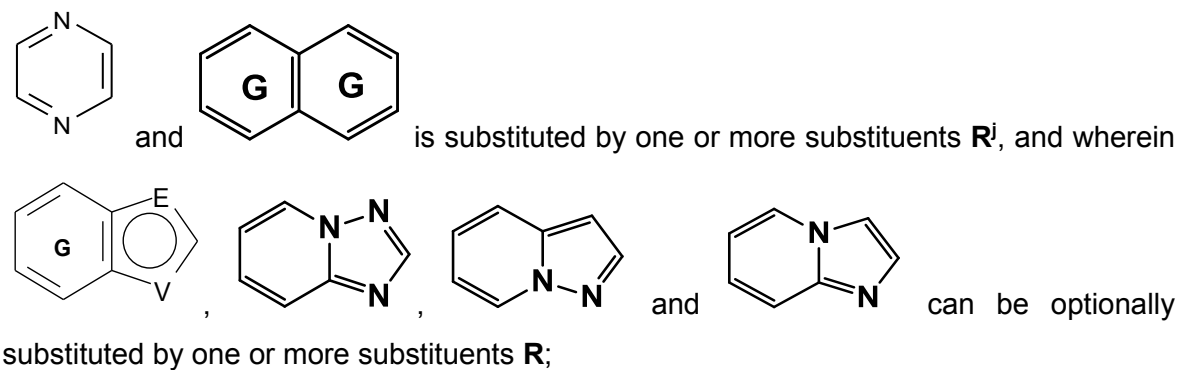
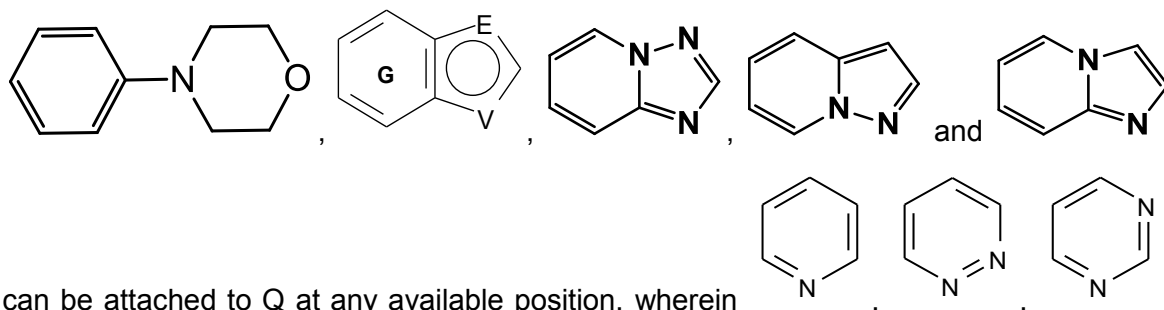
1. A compound of formula (I):



and all stereoisomers, racemic mixtures, tautomers, pharmaceutically acceptable salts, prodrugs, hydrates, solvates and polymorphs thereof;

wherein





B is selected from the group consisting of O and NR^a ;

E and **V** are independently selected from the group consisting of N, NR^5 , O and S;

G is selected from the group consisting of a benzene ring, a pyrimidine ring and a pyridine ring;

J is selected from the group consisting of O and $N-R^1$;

Q is selected from the group consisting of N and $C-R^1$;

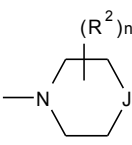
Y is selected from the group consisting of CZ and N, provided that when **Y** is N and Y^1 , Y^2 and Y^3 are CZ, **B** is N-alkyl or O;

Y^1 is selected from the group consisting of CZ and N;

Y^2 is selected from the group consisting of CZ and N;

Y^3 is selected from the group consisting of CZ and N;

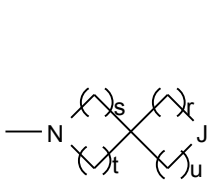
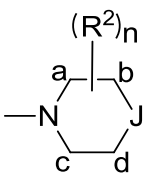
Z is independently selected from the group consisting of H, halogen, O-alkyl, alkyl and CN;

R is independently selected from the group consisting of  and $\text{--NR}^3\text{R}^4$;

R^a is selected from the group consisting of H and alkyl;

R^b, R^c, R^d, R^e, R^f, and R^g are independently selected from the group consisting of H and alkyl, or any two of **R^b, R^c, R^d, R^e, R^f, and R^g** may be joined to form a 3 to 8-membered ring;

R^j is independently selected from the group consisting of --halogen , --O-alkyl , --CF_3 , --CN ,

$\text{--NR}^3\text{R}^4$,  and , wherein a C₁₋₂ carbon atom-containing bridge can be present between the a carbon atom and the c or d carbon atom or wherein a C₁₋₂ carbon atom-containing bridge can be present between the b carbon atom and the c or d carbon atom;

R¹ is selected from the group consisting of H and alkyl;

R² is independently selected from the group consisting of alkyl, F and =O, wherein the alkyl can be optionally substituted by halogen, --OH or --O-alkyl and wherein if two **R²** are geminal they can be joined to form a 3 to 6-membered ring;

R³ and R⁴ are independently selected from the group consisting of H and alkyl, wherein the alkyl can be optionally substituted by halogen, --OH or --O-alkyl ;

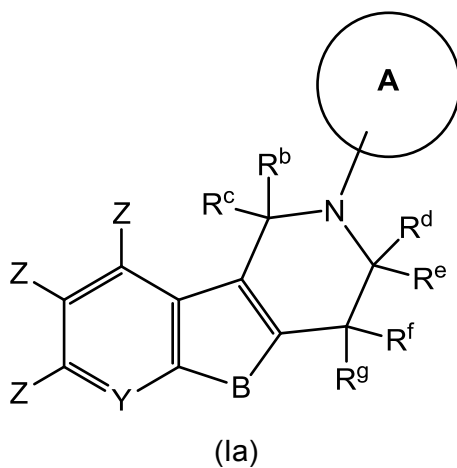
R⁵ is selected from the group consisting of H and alkyl;

n is 0, 1, 2, 3 or 4.

r and **s** are independently 0, 1, 2 or 3; and

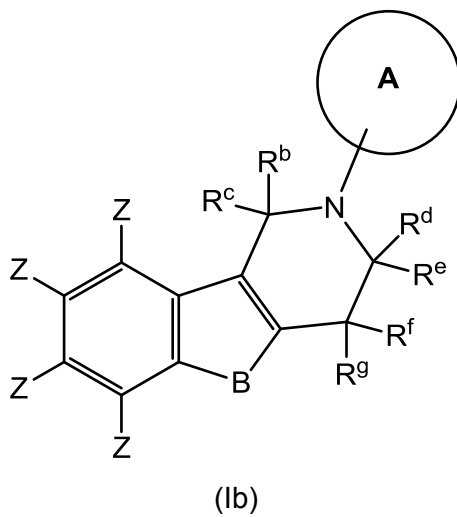
t and **u** are independently 1, 2 or 3.

2. The compound according to claim 1, which is a compound of formula (1a):



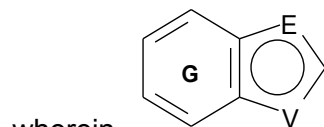
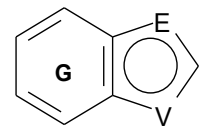
Wherein **A**, **B**, **R^b**, **R^c**, **R^d**, **R^e**, **R^f**, **R^g**, **Y** and **Z** are as defined in claim 1.

3. The compound according to claim 1, which is a compound of formula (1b):

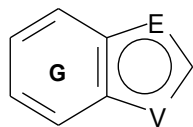


wherein **A**, **B**, **R^b**, **R^c**, **R^d**, **R^e**, **R^f**, **R^g** and **Z** are as defined in claim 1.

4. The compound according to any one of claims 1 to 3, wherein **A** is

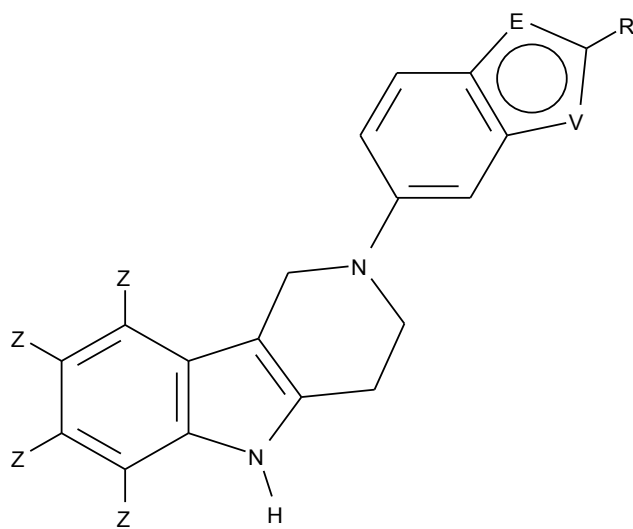


wherein can be attached to Q or to N at any available position, and



wherein can be optionally substituted by one or more substituents **R**.

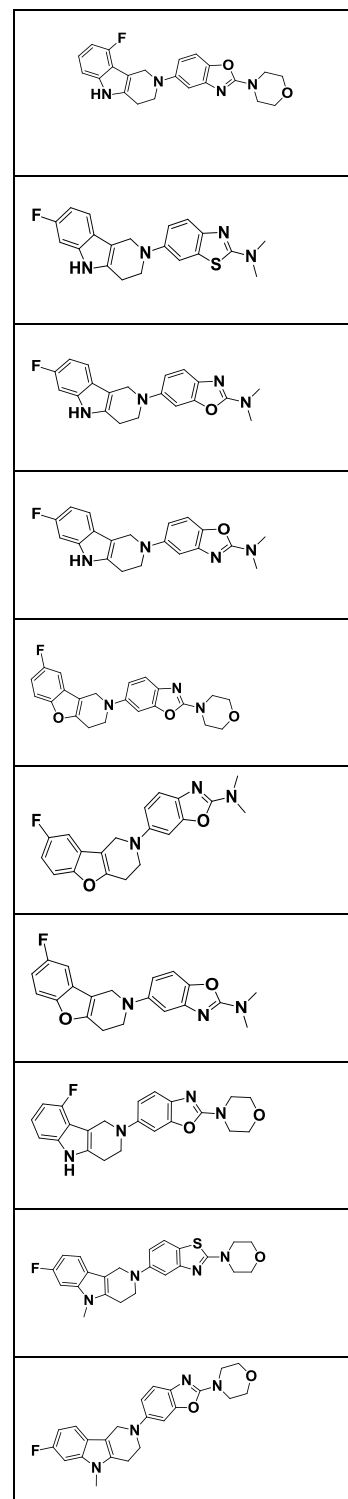
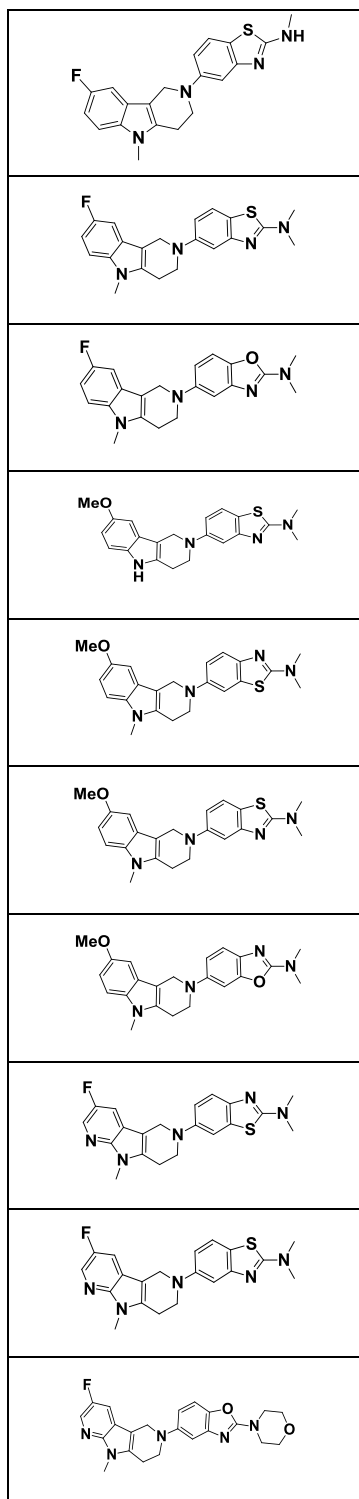
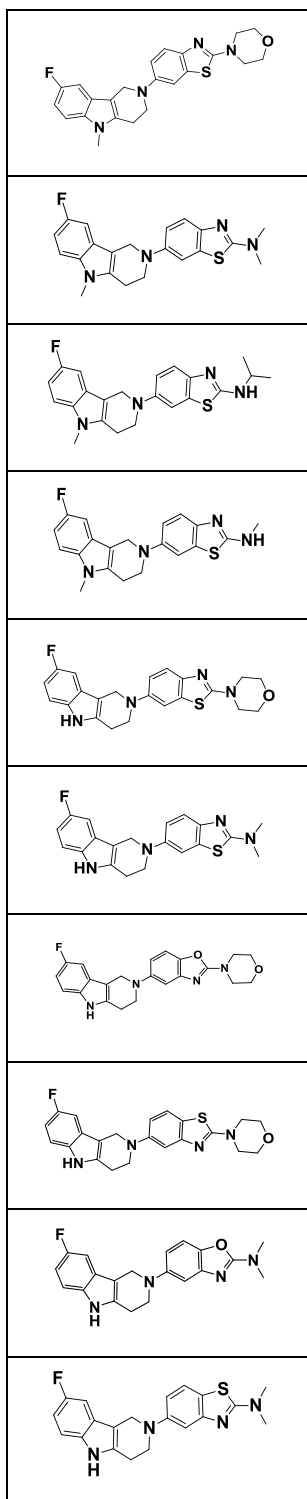
5. The compound according to any one of claims 1 to 4, which is a compound of the formula (Ic):

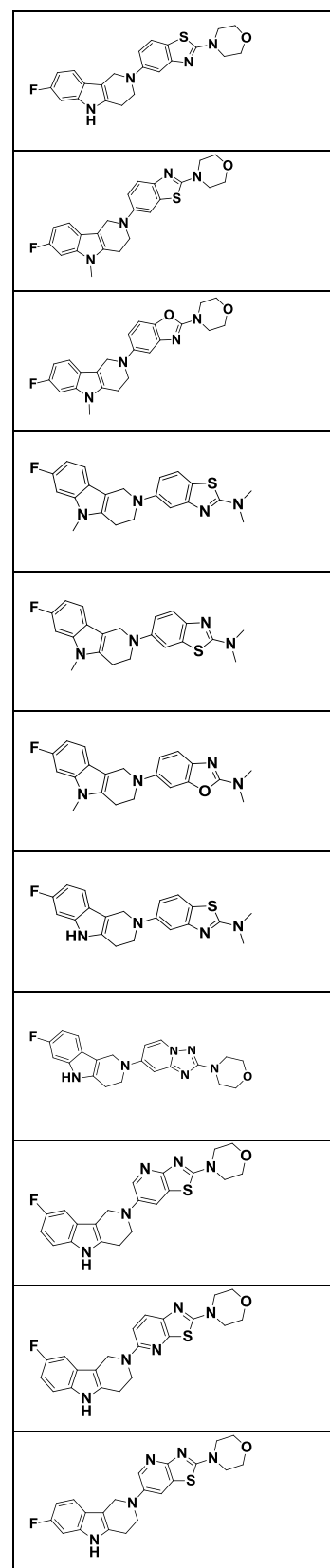
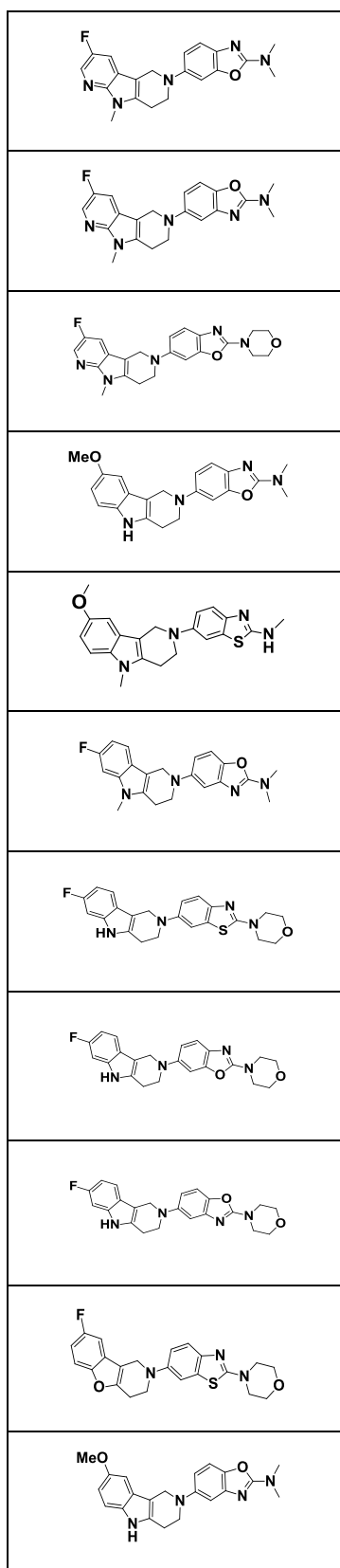
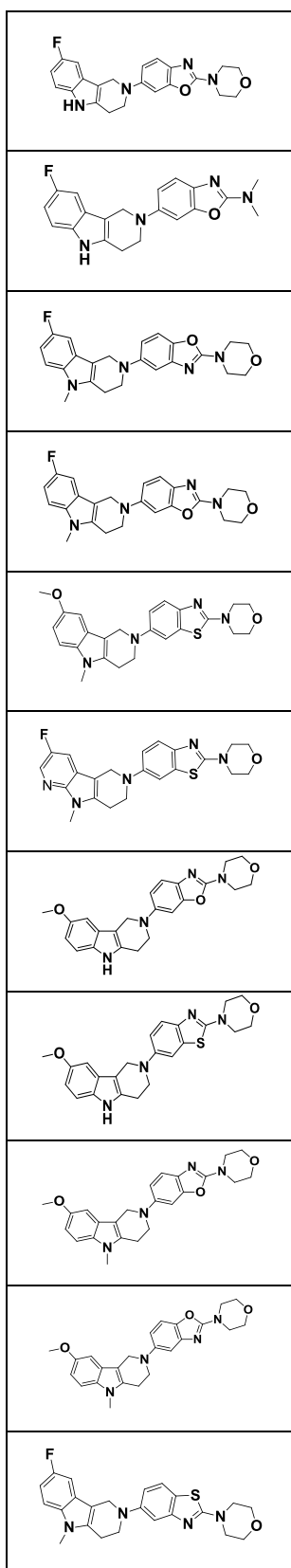


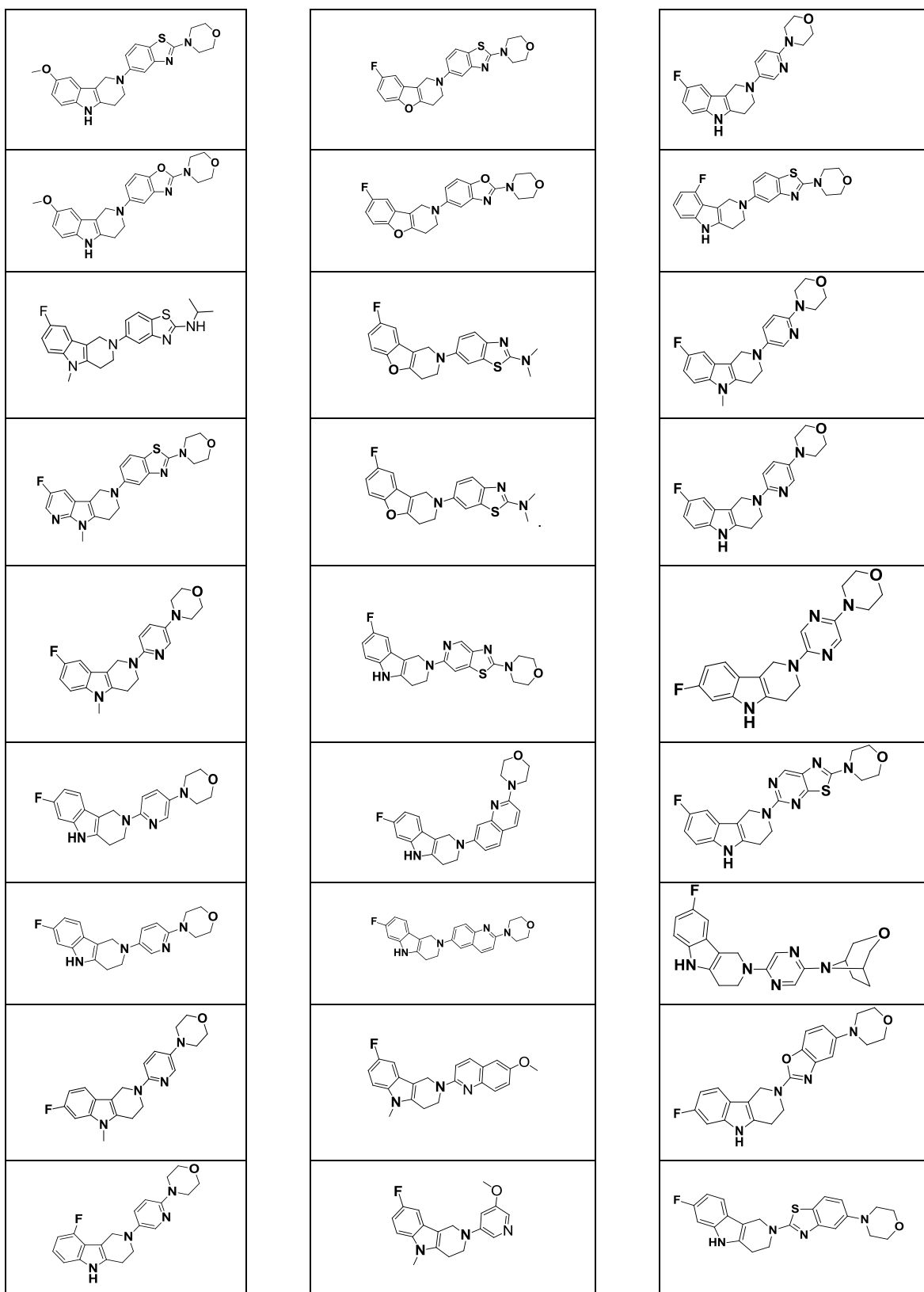
(Ic)

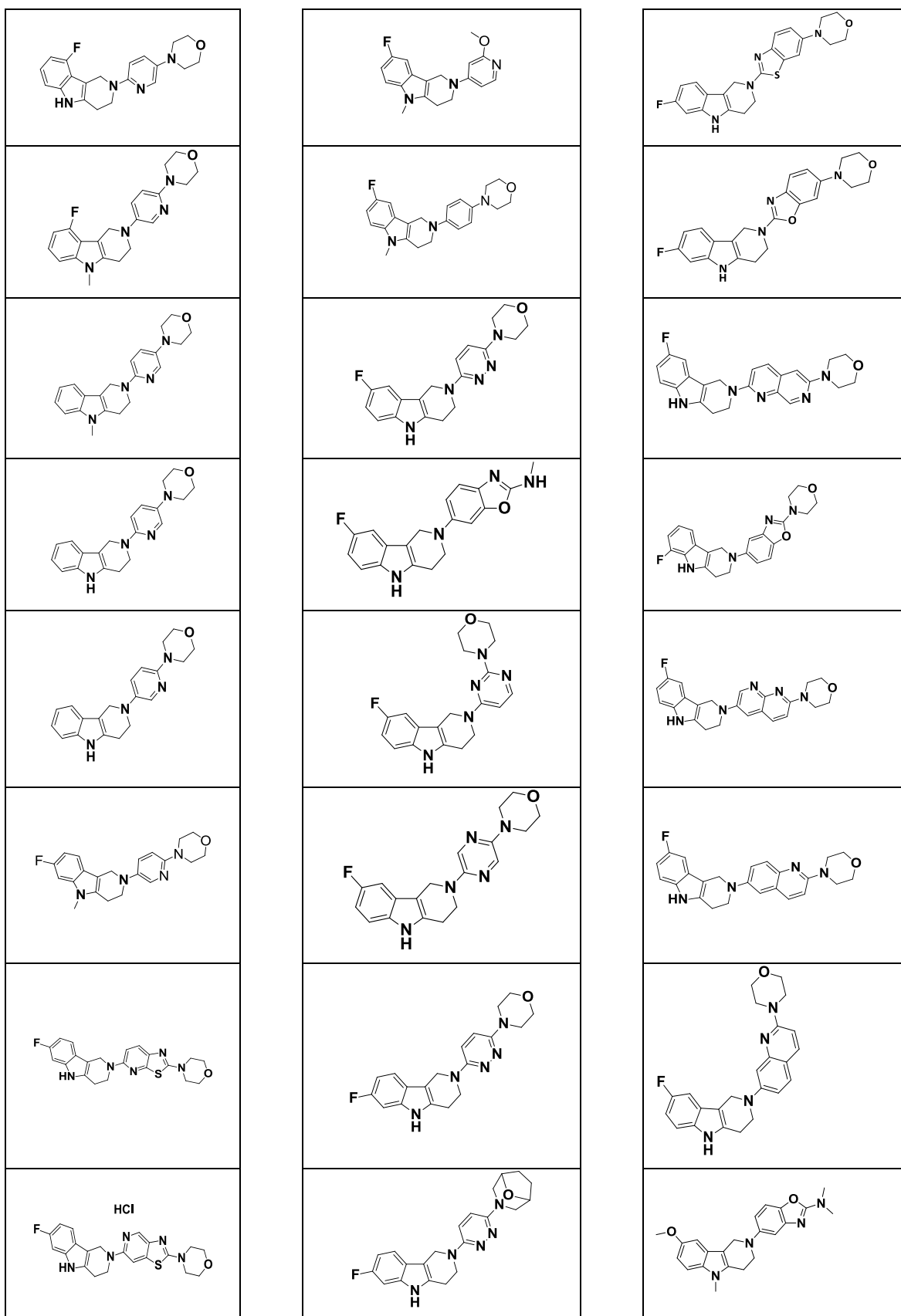
wherein **E**, **R**, **V** and **Z** are as defined in claim 1.

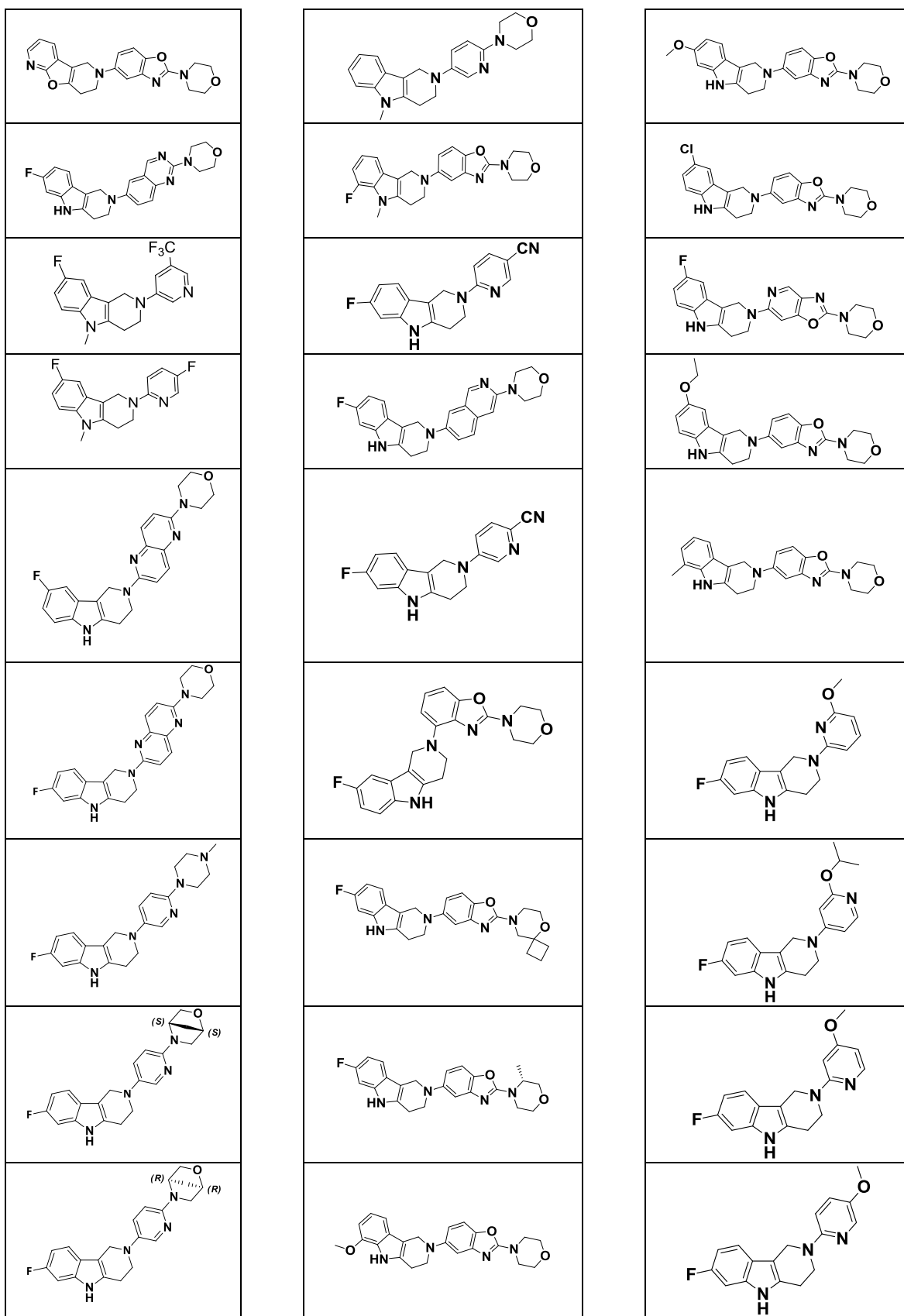
6. The compound according to claim 1, wherein the compound is selected from the group consisting of

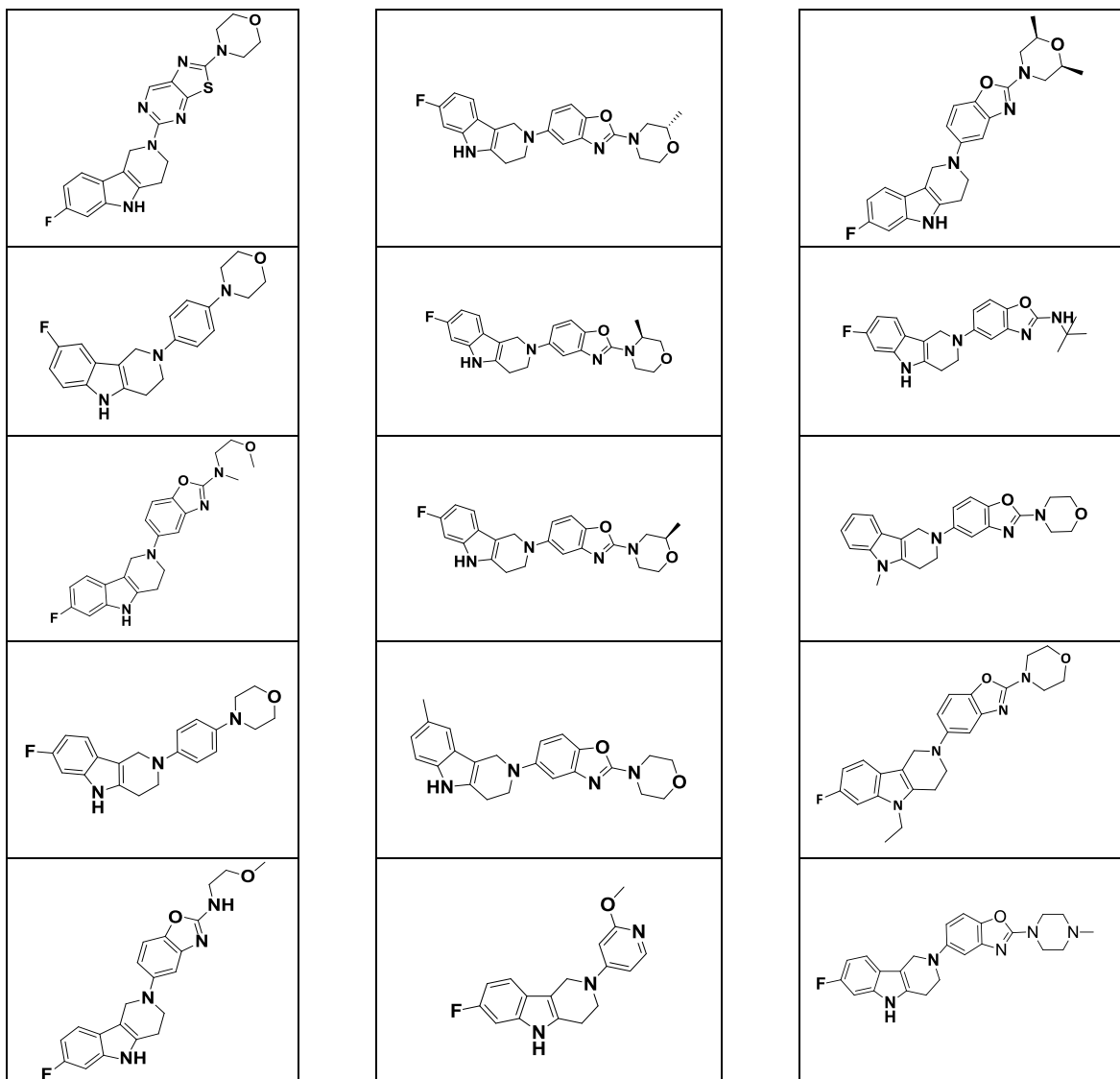






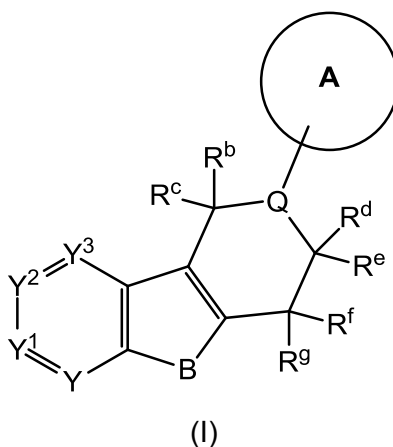






7. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 6 and optionally a pharmaceutically acceptable carrier or excipient.
8. The compound as defined in any one of claims 1 to 6, for use as a medicament.

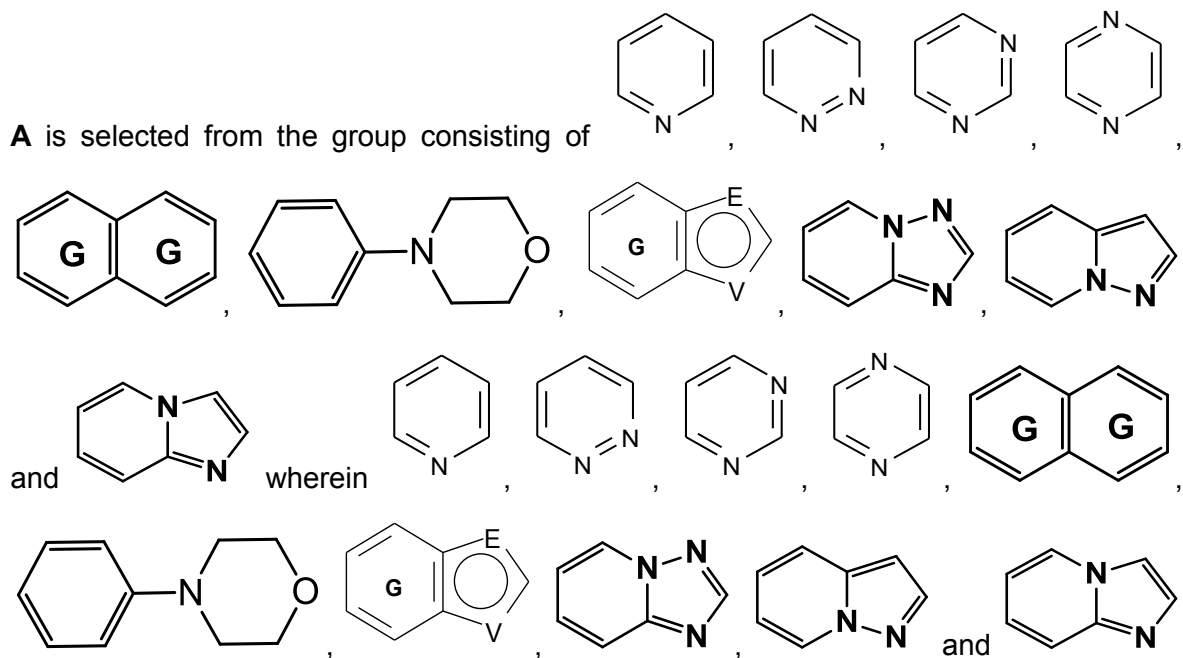
9. A compound of formula (I):



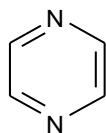
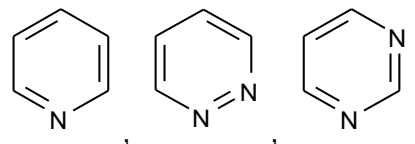
and all stereoisomers, racemic mixtures, tautomers, pharmaceutically acceptable salts, prodrugs, hydrates, solvates and polymorphs thereof;

for use in the treatment, alleviation or prevention of a disorder or abnormality associated with Tau protein aggregates,

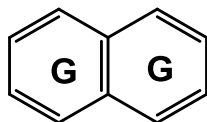
wherein



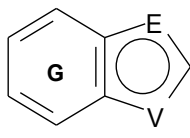
can be attached to Q at any available position, wherein



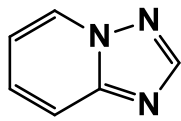
and



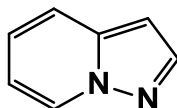
is substituted by one or more substituents R^j , and wherein



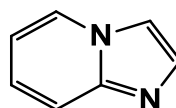
,



,



and



can be optionally

substituted by one or more substituents R ;

B is selected from the group consisting of O and NR^a ;

E and **V** are independently selected from the group consisting of N, NR^5 , O and S;

G is selected from the group consisting of a benzene ring, a pyrimidine ring and a pyridine ring;

J is selected from the group consisting of O and $N-R^1$;

Q is selected from the group consisting of N and $C-R^1$;

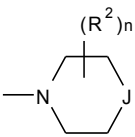
Y is selected from the group consisting of CZ and N;

Y¹ is selected from the group consisting of CZ and N;

Y² is selected from the group consisting of CZ and N;

Y³ is selected from the group consisting of CZ and N;

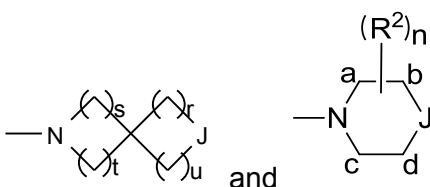
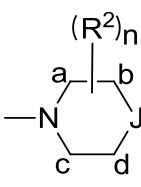
Z is independently selected from the group consisting of H, halogen, O-alkyl, alkyl and CN;

R is independently selected from the group consisting of  and $\text{--NR}^3\text{R}^4$;

R^a is selected from the group consisting of H and alkyl;

R^b, R^c, R^d, R^e, R^f, and R^g are independently selected from the group consisting of H and alkyl, or any two of **R^b, R^c, R^d, R^e, R^f, and R^g** may be joined to form a 3 to 8-membered ring;

R^j is independently selected from the group consisting of --halogen , --O--alkyl , --CF_3 , --CN ,

$\text{--NR}^3\text{R}^4$,  and , wherein a C₁₋₂ carbon atom-containing bridge can be present between the a carbon atom and the c or d carbon atom or wherein a C₁₋₂ carbon atom-containing bridge can be present between the b carbon atom and the c or d carbon atom;

R¹ is selected from the group consisting of H and alkyl;

R² is independently selected from the group consisting of alkyl, F and =O, wherein the alkyl can be optionally substituted by halogen, --OH or --O--alkyl and wherein if two **R²** are geminal they can be joined to form a 3 to 6-membered ring;

R³ and R⁴ are independently selected from the group consisting of H and alkyl, wherein the alkyl can be optionally substituted by halogen, --OH or --O--alkyl ;

R⁵ is selected from the group consisting of H and alkyl;

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

r and **s** are independently 0, 1, 2 or 3; and

t and **u** are independently 1, 2 or 3.

10. The compound for use according to claim 9, wherein the compound of formula (I) is as defined in any one of claims 1 to 6.
11. Use of a compound as defined in any of claims 1 to 6 or 9, in the manufacture of a medicament for treating, preventing or alleviating a disorder or abnormality associated with Tau protein aggregates.
12. The compound for use according to claim 9, or the use according to claim 11, wherein the disorder is selected from Alzheimer's disease (AD), familial AD, Primary Age-Related Tauopathy (PART), Creutzfeldt-Jacob disease, dementia pugilistica, Down's Syndrome, Gerstmann-Sträussler-Scheinker disease (GSS), inclusion-body myositis, prion protein cerebral amyloid angiopathy, traumatic brain injury (TBI), amyotrophic lateral sclerosis (ALS), Parkinsonism-dementia complex of Guam, non-Guamanian motor neuron disease with neurofibrillary tangles, argyrophilic grain disease, corticobasal degeneration (CBD), diffuse neurofibrillary tangles with calcification, frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), Hallervorden-Spatz disease, multiple system atrophy (MSA), Niemann-Pick disease type C, pallido-ponto-nigral degeneration, Pick's disease (PiD), progressive subcortical gliosis, progressive supranuclear palsy (PSP), subacute sclerosing panencephalitis, tangle predominant dementia, postencephalitic Parkinsonism, myotonic dystrophy, subacute sclerosis panencephalopathy, mutations in LRRK2, chronic traumatic encephalopathy (CTE), familial British dementia, familial Danish dementia, other frontotemporal lobar degenerations, Guadeloupean Parkinsonism, neurodegeneration with brain iron accumulation, SLC9A6-related mental retardation, white matter tauopathy with globular glial inclusions, epilepsy, Lewy body dementia (LBD), mild cognitive impairment (MCI), multiple sclerosis, Parkinson's disease, HIV-related dementia, adult onset diabetes, senile cardiac amyloidosis, glaucoma, ischemic stroke, psychosis in AD and Huntington's

disease, preferably Alzheimer's disease (AD), corticobasal degeneration (CBD), Pick's disease (PiD), and progressive supranuclear palsy (PSP).

13. The compound as defined in any one of claims 1 to 6 or 9, for use in decreasing Tau aggregation.
14. The compound as defined in any one of claims 1 to 6 or 9, for use in preventing the formation of Tau aggregates and/or for use in inhibiting Tau aggregation.
15. The compound as defined in any one of claims 1 to 6 or 9, for use in interfering intracellularly with Tau aggregates.
16. The compound as defined in any one of claims 1 to 6 or 9, for use in reducing Tau misfolding and hyperphosphorylation *in vivo*.
17. The compound as defined in any one of claims 1 to 6 or 9, for use in reducing neuroinflammatory markers.

18. Use of a compound as defined in any of claims 1 to 6 or 9, in the manufacture of a medicament for decreasing Tau aggregation.
19. Use of a compound as defined in any of claims 1 to 6 or 9, in the manufacture of a medicament for preventing the formation of Tau aggregates and/or for inhibiting Tau aggregation.
20. Use of a compound as defined in any of claims 1 to 6 or 9, in the manufacture of a medicament for interfering intracellularly with Tau aggregates.
21. Use of a compound as defined in any of claims 1 to 6 or 9, in the manufacture of a medicament for reducing Tau misfolding and hyperphosphorylation *in vivo*.
22. Use of a compound as defined in any of claims 1 to 6 or 9, in the manufacture of a medicament for reducing neuroinflammatory markers.
23. A mixture comprising a compound as defined in any one of claims 1 to 6 and at least one further biologically active compound selected from a therapeutic agent different from the compound as defined in any one of claims 1 to 6, wherein the mixture further comprises at least one of a pharmaceutically acceptable carrier, a diluent and an excipient.
24. The mixture according to claim 23, wherein the compound and/or the further biologically active compound is/are present in a therapeutically effective amount.
25. The mixture according to claim 23 or 24, wherein the further biologically active compound is selected from the group consisting of compounds against oxidative stress, anti-apoptotic compounds, metal chelators, inhibitors of DNA repair such as pirenzepine and metabolites, 3-amino-1-propanesulfonic acid (3APS), 1,3-propanedisulfonate (1,3PDS), α -secretase activators, β - and γ -secretase inhibitors, glycogen synthase kinase 3 inhibitors,

O-glucanase (OGA) inhibitors, neurotransmitter, β -sheet breakers, attractants for amyloid beta clearing / depleting cellular components, inhibitors of N-terminal truncated amyloid beta including pyroglutamated amyloid beta 3-42, anti-inflammatory molecules, or cholinesterase inhibitors (ChEIs) such as tacrine, rivastigmine, donepezil, and/or galantamine, M1 agonists, other drugs including any amyloid or Tau modifying drug and nutritive supplements, an antibody, including any functionally equivalent antibody or functional parts thereof or a vaccine.

26. The mixture according to claim 25, wherein the further biologically active compound is a cholinesterase inhibitor (ChEI).
27. The mixture according to claim 25, wherein the further biologically active compound is selected from the group consisting of tacrine, rivastigmine, donepezil, galantamine, niacin and memantine.
28. The mixture according to claim 25, wherein the further biologically active compound is an antibody, particularly a monoclonal antibody, including any functionally equivalent antibody or functional parts thereof.
29. The mixture according to any one of claims 23 to 28, wherein the compound and/or the further biologically active compound is/are present in a therapeutically effective amount.
30. Use of the compound as defined in any of claims 1 to 6 or 9 as an analytical reference or an *in vitro* screening tool.