Different physiochemical and biological properties (e.g. pharmacokinetic profile, efficacy in inhibition/reduction of protein aggregation, reversibility of target binding) are desired in compounds for therapeutic use in treatment, prevention or alleviation of neurodegenerative diseases characterized by pathological protein accumulation (proteinopathies) compared to compounds for use in imaging of such diseases.

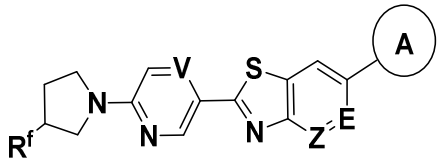
The development of disease-modifying drug therapies for PD and other synucleinopathies would address an unmet medical need since currently only symptomatic treatments are available (McFarthing et al., J Parkinsons Dis. 2022;12(4):1073-1082). Therefore, there remains a need for identifying novel therapeutic agents that can inhibit the accumulation and spreading of alpha-synuclein.

SUMMARY

The present disclosure provides compounds that can be employed in the treatment, alleviation or prevention of a disease, disorder or abnormality associated with alpha-synuclein aggregates (such as Parkinson's disease). The disclosure further provides methods of treating, alleviation, or preventing diseases, disorders and abnormalities associated with alpha-synuclein aggregates.

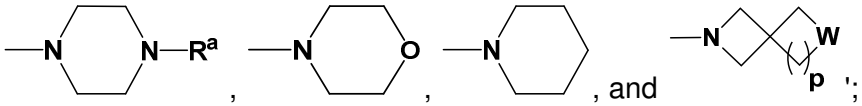
Compounds according to the disclosure described herein can bind specifically to aggregated alpha-synuclein species acting as “seeds” and inhibit and/or delay the accumulation of pathological alpha-synuclein intracellularly as well as the transsynaptic transmission, seeding, and spreading of alpha-synuclein aggregated species in the brain. Due to their unique design features, these compounds display properties such as appropriate lipophilicity, molecular weight, solubility, permeability and metabolic stability, which result in cell penetration, oral bioavailability, and brain uptake, adequate to be a successful medicament for the treatment, alleviation or prevention of diseases, disorders or abnormalities associated with alpha-synuclein aggregates.

Various examples of the disclosure are described herein. In one aspect, provided herein is a compound of formula (I):


(I)

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein


is selected from the group consisting of


;

wherein 
is optionally substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -C_1-C_3alkyl, -OC_1-C_3alkyl, -N$\mathbf{R^b}\mathbf{R^c}$, spiro-cycloalkyl including 3 to 6 ring atoms, and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O;

W is selected from N$\mathbf{R^a}$ and C$\mathbf{R^d}\mathbf{R^e}$;

p is 1 or 2;

for each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$;

for each occurrence $\mathbf{R^d}$ is selected from hydrogen, -OH, and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^e}$ is selected from hydrogen and C_1-C_3 alkyl;

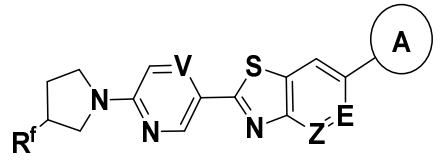
V is selected from CH or N;

Z is selected from CH or N;

E is selected from CH or N; wherein at least one of **Z** and **E** is CH; and

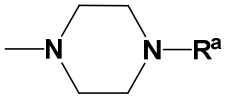
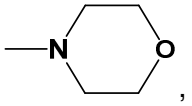
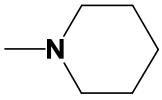
$\mathbf{R^f}$ is selected from hydrogen, --OC_1-C_3alkyl and halogen.

Within a certain example, provided herein is a compound of formula (I):


(I)

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein


is selected from the group consisting of


, 
, 
; and 
.

Optionally 
can be substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -C_1-C_3alkyl, -OC_1-C_3alkyl, -N$\mathbf{R^bR^c}$, spiro-cycloalkyl including 3 to 6 ring atoms, and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O.

W is selected from N$\mathbf{R^a}$ and C$\mathbf{R^dR^e}$

p is 1 or 2.

For each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl.

For each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl.

For each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$.

For each occurrence $\mathbf{R^d}$ is selected from hydrogen, -OH, and C_1-C_3 alkyl.

For each occurrence $\mathbf{R^e}$ is selected from hydrogen and C_1-C_3 alkyl.

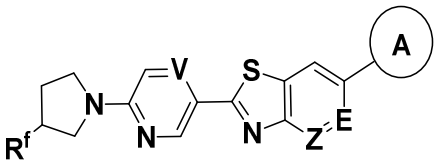
V is selected from CH or N.

Z is selected from CH or N.

E is selected from CH or N; wherein at least one of **Z** and **E** is CH.

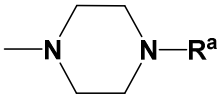
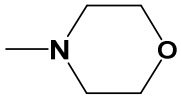
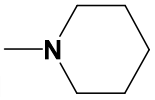
$\mathbf{R^f}$ is selected from hydrogen, -OC_1-C_3alkyl and halogen.

In another aspect, the disclosure is also directed to a compound of formula (I'):


(I')

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein


is selected from the group consisting of


, 
, and 
;

wherein 
is optionally substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -$\mathbf{NR^bR^c}$, spiro-cycloalkyl including 3 to 6 ring atoms, and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O;

for each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$;

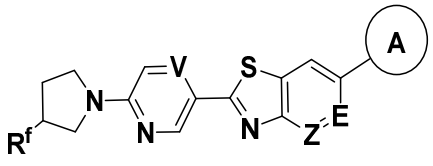
V is selected from CH or N;

Z is selected from CH or N;

E is selected from CH or N; wherein at least one of **Z** and **E** is CH; and

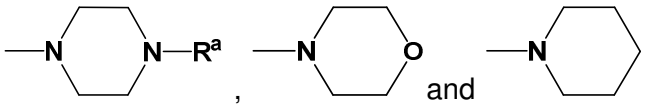
$\mathbf{R^f}$ is selected from hydrogen and halogen.

In another example, the disclosure is also directed to a compound having the following subformula (I'):


(I')

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof.


is selected from the group consisting of


, and .

Optionally  can be substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -$\mathbf{NR^bR^c}$, spiro-cycloalkyl including 3 to 6 ring atoms and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O.

For each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl.

For each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl.

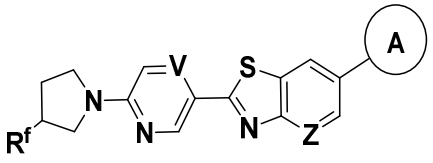
For each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$.

Z is selected from CH or N and **E** is selected from CH or N; wherein at least one of **Z** and **E** is CH;

V is selected from CH or N.

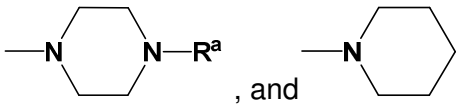
$\mathbf{R^f}$ is selected from hydrogen and halogen.

In another example, the disclosure is also directed to a compound having the following subformula (I"):


(I")

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein


is selected from the group consisting of


; and

wherein  is optionally substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -$\mathbf{NR^bR^c}$, and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O;

for each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl;

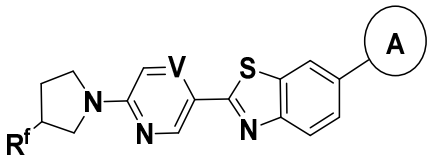
for each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$;

Z is selected from CH or N;

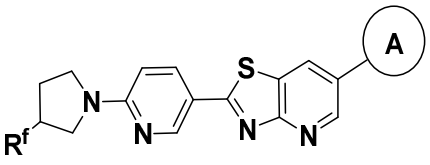
V is selected from CH or N;

and $\mathbf{R^f}$ is selected from hydrogen and halogen.

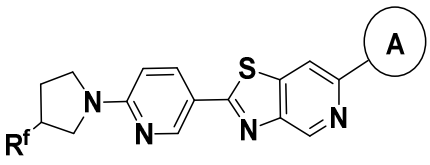
In another example, the disclosure is also directed to a compound having the following subformulae



(Ia),



(Ib),



(Ic),

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof,

wherein 

, **V** and $\mathbf{R^f}$ are as defined above.

In another aspect, the disclosure provides a pharmaceutical composition comprising a compound according to the disclosure, and optionally at least one pharmaceutically acceptable excipient, carrier, diluent and/or adjuvant.

In another example, the disclosure provides a pharmaceutical composition comprising a compound according to the definition of compound of formula (I), and optionally a pharmaceutically acceptable carrier, diluent, adjuvant and/or excipient.

In another example, the disclosure provides a compound of formula (I), or a combination, in particular a pharmaceutical composition, as disclosed herein, for use as a medicament.

In another example, the disclosure provides a compound of formula (I), as disclosed herein, or a pharmaceutical composition, for use in the treatment, alleviation or prevention of a disease, disorder or abnormality associated alpha-synuclein aggregates.

In another example, the disclosure provides a method of treating, alleviating or preventing a disease, disorder or abnormality associated with alpha-synuclein aggregates comprising administering a compound of formula (I), as disclosed herein, or a pharmaceutical composition, to a subject in need thereof.

In another aspect, the disclosure provides a use of the compound according to the disclosure, or the pharmaceutical composition according to the disclosure, in the manufacture of a medicament for the prevention, alleviation or treatment of a disease, disorder or abnormality associated with alpha-synuclein aggregates.

In another aspect, the disclosure provides a use of the compound according to the disclosure, in the manufacture of a medicament for inhibiting or preventing alpha-synuclein aggregation.

In another aspect, the disclosure provides a use of the compound according to the disclosure, in the manufacture of a medicament for reducing the concentration of alpha-synuclein aggregates.

In another aspect, the disclosure provides a use of the compound according to the disclosure, in the manufacture of a medicament for inhibiting *de novo* alpha-synuclein aggregate formation.

In another aspect, the disclosure provides a use of the compound according to the disclosure as an *in vitro* analytical reference or an *in vitro* screening tool.

In another aspect, the disclosure provides a mixture or a combination comprising a compound according to the disclosure, and one or more therapeutic agent(s) different from the compound as defined according to the disclosure, and optionally a pharmaceutically acceptable carrier, diluent, adjuvant and/or excipient.

In another example, the disclosure provides the use of a compound of formula (I), as disclosed herein, for the manufacture of a medicament for treating, alleviating or preventing a disease, disorder or abnormality associated with alpha-synuclein aggregates.

In some examples, the disease, disorder or abnormality is selected from Parkinson's disease (including sporadic, familial with alpha-synuclein mutations, familial with mutations other than alpha-synuclein, pure autonomic failure or Lewy body dysphagia), SNCA duplication carrier, Lewy Body dementia (LBD), dementia with Lewy bodies (DLB) (including “pure” Lewy body dementia), Parkinson’s disease dementia (PDD), diffuse Lewy body disease (DLBD), Alzheimer’s disease, sporadic Alzheimer’s disease, familial Alzheimer's disease with APP mutations, familial Alzheimer's disease with PS-1, PS-2 or other mutations, familial British dementia, Lewy body variant of Alzheimer’s disease, Down syndrome, multiple system atrophy (MSA) (including Shy-Drager syndrome, striatonigral degeneration or olivopontocerebellar atrophy), traumatic brain injury, chronic traumatic encephalopathy, dementia puglistica, tauopathies (including Pick's disease, frontotemporal dementia, progressive supranuclear palsy, corticobasal degeneration, Niemann-Pick type C1 disease, frontotemporal dementia with Parkinsonism linked to chromosome 17), Creutzfeldt-Jakob disease, Huntington's disease, motor neuron disease, amyotrophic lateral sclerosis (including sporadic, familial or ALS-dementia complex of Guam), neuroaxonal dystrophy, neurodegeneration with brain iron accumulation type 1 (including Hallervorden-Spatz syndrome), prion diseases, ataxia telangiectatica, Meige’s syndrome, subacute sclerosing panencephalitis, Gerstmann-Straussler-Scheinker disease, inclusion-body myositis, Gaucher disease, Krabbe disease as well as other lysosomal storage disorders (including Kufor-Rakeb syndrome and Sanfilippo syndrome) and rapid eye movement (REM) sleep behavior disorder.

In another example, the disclosure provides a compound of formula (I), as defined herein, for use as an *in vitro* analytical reference or an *in vitro* screening tool.

In another example, the disclosure provides a combination comprising a compound of formula (I), as defined herein, and one or more therapeutic agents different from the compound of formula (I).

In another example, the disclosure provides a mixture comprising a compound of formula (I), as defined herein, and one or more therapeutic agents different from the compound of formula (I).

DEFINITIONS

For the purpose of interpreting this specification, the following definitions will apply unless specified otherwise, and when appropriate, terms used in the singular will also include the plural and vice versa. It must also be noted that as used herein and in the appended claims, the singular forms "a", "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "the compound" includes reference to one or more compounds; and so forth.

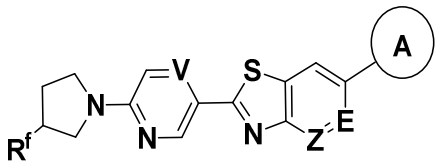
The term "C_1-C_3 alkyl" refers to a saturated straight or branched hydrocarbon chain consisting solely of carbon and hydrogen atoms containing no unsaturation, having from one to three carbon atoms, and which is attached to the rest of the molecule by a single bond. Examples of suitable alkyl groups having 1 to 3 carbon atoms include, but are not limited to, methyl, ethyl, propyl, isopropyl, 1-methylethyl.

The term "heterocycloalkyl" refers to a stable 3- to 8-membered saturated monocyclic ring radical which comprises 1 heteroatom which is selected from N, O or S. The heterocycloalkyl group may be bonded via a carbon atom or a heteroatom, preferably by a carbon atom. Examples include, but are not limited to, aziridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, pyrrolidinyl, tetrahydrofuryl, tetrahydrothienyl, piperidyl, tetrahydropyranyl, perhydroazepinyl, azepanyl, or azocanyl, preferably azetidinyl, oxetanyl, thietanyl, pyrrolidinyl, tetrahydrofuryl, and piperidyl, more preferably oxetanyl.

The term "spiro-heterocycloalkyl" refers to a heterocycloalkyl moiety which is attached in a spiro manner, i.e., the heterocycloalkyl ring and the ring to which it is attached have a common ring atom.

CLAIMS

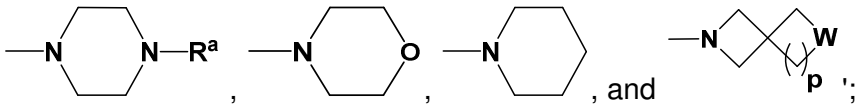
1. A compound of formula (I):



(I)

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein

 is selected from the group consisting of



; wherein  is optionally substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -C_1-C_3alkyl, -OC_1-C_3alkyl, -N$\mathbf{R^bR^c}$, spiro-cycloalkyl including 3 to 6 ring atoms, and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O;

W is selected from N$\mathbf{R^a}$ and C$\mathbf{R^dR^e}$;

p is 1 or 2;

for each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$;

for each occurrence $\mathbf{R^d}$ is selected from hydrogen, -OH, and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^e}$ is selected from hydrogen and C_1-C_3 alkyl;

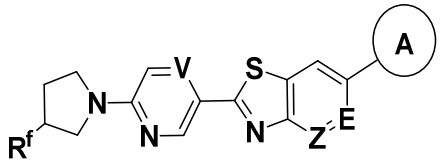
V is selected from CH or N;

Z is selected from CH or N;

E is selected from CH or N; wherein at least one of **Z** and **E** is CH; and

$\mathbf{R^f}$ is selected from hydrogen, --OC_1-C_3alkyl and halogen.

2. A compound of formula (I'):

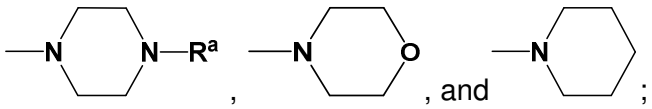


(I')

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein



is selected from the group consisting of



; wherein  is optionally substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -$\mathbf{NR^bR^c}$, spiro-cycloalkyl including 3 to 6 ring atoms, and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O;

for each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$;

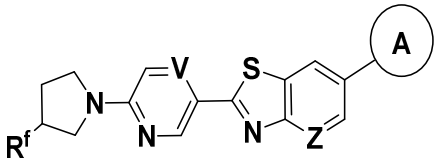
V is selected from CH or N;

Z is selected from CH or N;

E is selected from CH or N; wherein at least one of **Z** and **E** is CH; and

$\mathbf{R^f}$ is selected from hydrogen and halogen.

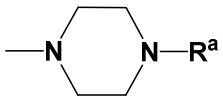
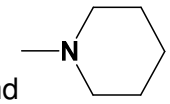
3. A compound according to claim 1 or 2, having a formula (I"):



(I")

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein


is selected from the group consisting of


, and

;

wherein  is optionally substituted at any available position by one to three substituents $\mathbf{R^A}$, wherein each $\mathbf{R^A}$ is independently selected from the group consisting of -OH, halogen, -$\mathbf{NR^bR^c}$, and spiro-heterocycloalkyl including 3 to 6 ring atoms wherein 1 ring atom is O;

for each occurrence $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl;

for each occurrence $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl;

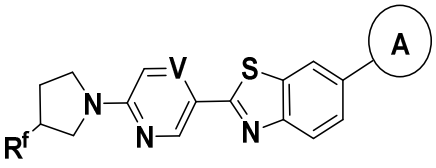
for each occurrence $\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is selected from O, S and N$\mathbf{R^a}$;

Z is selected from CH or N;

V is selected from CH or N; and

$\mathbf{R^f}$ is selected from hydrogen and halogen.

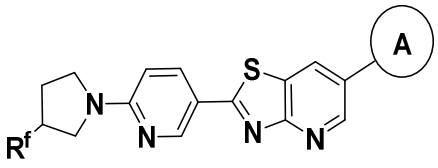
4. The compound according to any one of claims 1 to 3, having a formula (Ia):


(Ia),

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof,

wherein  , **V** and $\mathbf{R^f}$ are as defined in any one of claims 1 to 3.

5. The compound according to any one of claims 1 to 3, having a formula (Ib):



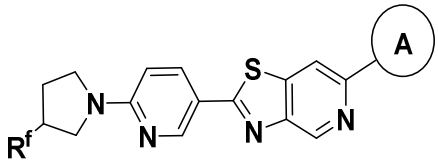
(Ib),

or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof,

wherein 

and $\mathbf{R^f}$ are as defined in any one of claims 1 to 3.

6. The compound according to claim 1 or 2, having a formula (Ic):



(Ic),

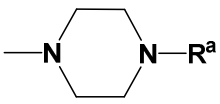
or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof,

wherein 

and $\mathbf{R^f}$ are as defined in claim 1 or 2.

7. The compound according to any one of claims 1 to 6, wherein

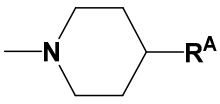


is selected from 

, wherein $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl.

8. The compound according to any one of claims 1 to 6, wherein

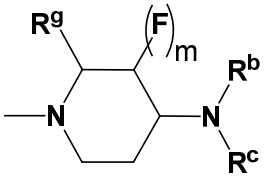


is selected from 

wherein $\mathbf{R^A}$ is independently selected from the group consisting of -OH and -$\mathbf{NR^bR^c}$; wherein $\mathbf{R^b}$ is selected from hydrogen and C_1-C_3 alkyl; and

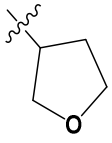
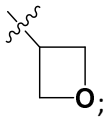
$\mathbf{R^c}$ is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is O.

9. The compound according to according to any one of claims 1 to 6, wherein


is selected from 

wherein

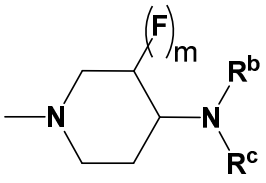
R^b is as defined in claim 1;

R^c is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is O, preferably **R^c** is selected from hydrogen,  and ;

R^g is selected from hydrogen and C_1-C_3 alkyl; and

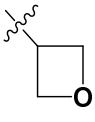
m is 0, 1 or 2.

10. The compound according to claim 9 wherein


is selected from 

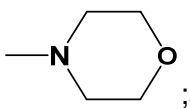
wherein

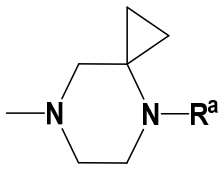
R^b is selected from hydrogen and C_1-C_3 alkyl, and

R^c is selected from hydrogen and heterocycloalkyl including from 3 to 8 ring atoms wherein one ring atom is O, preferably **R^c** is selected from hydrogen or ; and

m is 0, 1 or 2.

11. The compound according to according to any one of claims 1 to 6, wherein


is selected from ;and

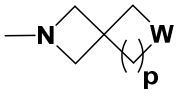


, wherein $\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl.

12. The compound according to any one of claim 1 to 6, wherein



is selected from



wherein

W is selected from N$\mathbf{R^a}$ and C$\mathbf{R^dR^e}$;

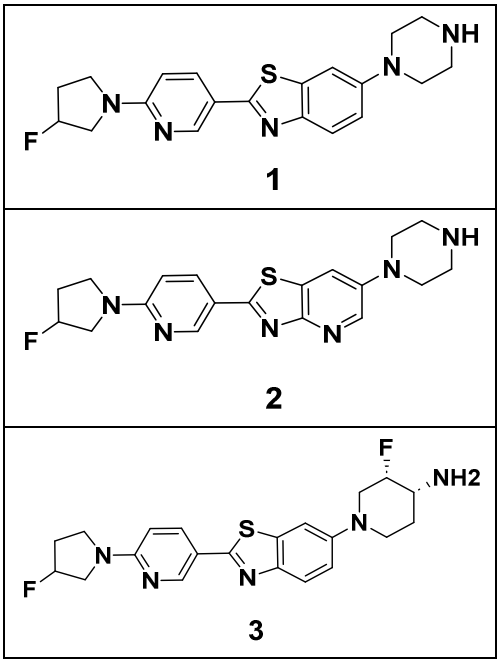
p is 1 or 2;

$\mathbf{R^a}$ is selected from hydrogen and C_1-C_3 alkyl, preferably hydrogen;

$\mathbf{R^d}$ is selected from hydrogen, -OH, and C_1-C_3 alkyl, preferably -OH; and

$\mathbf{R^e}$ is selected from hydrogen and C_1-C_3 alkyl, preferably -hydrogen.

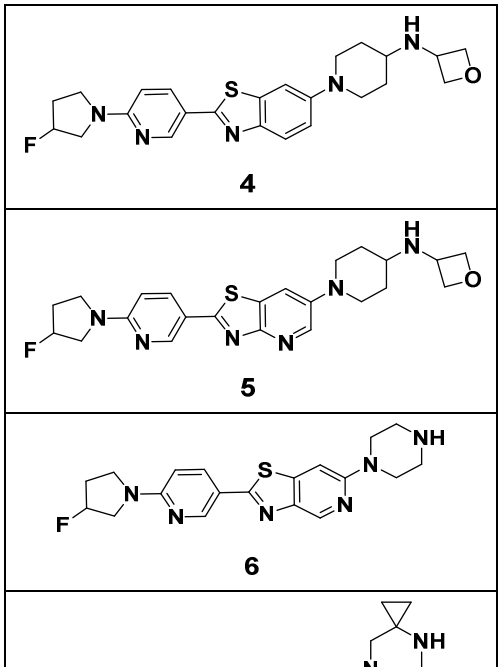
13. The compound according to claim 1, wherein the compound is selected from:



1

2

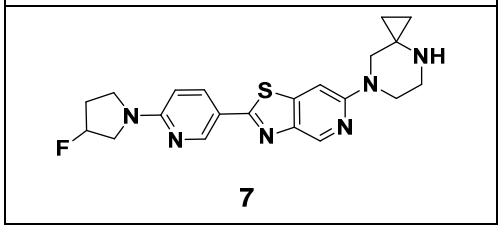
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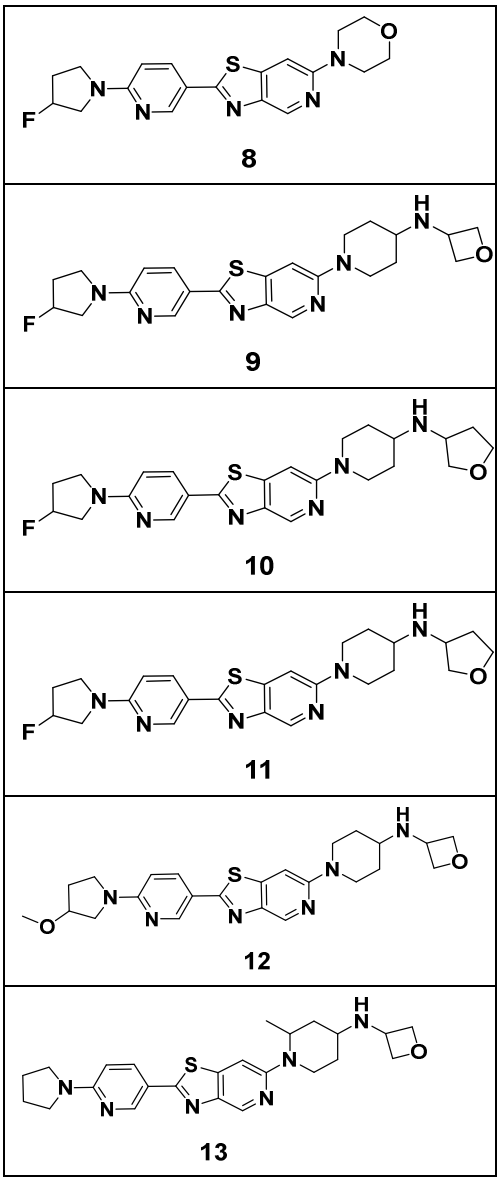
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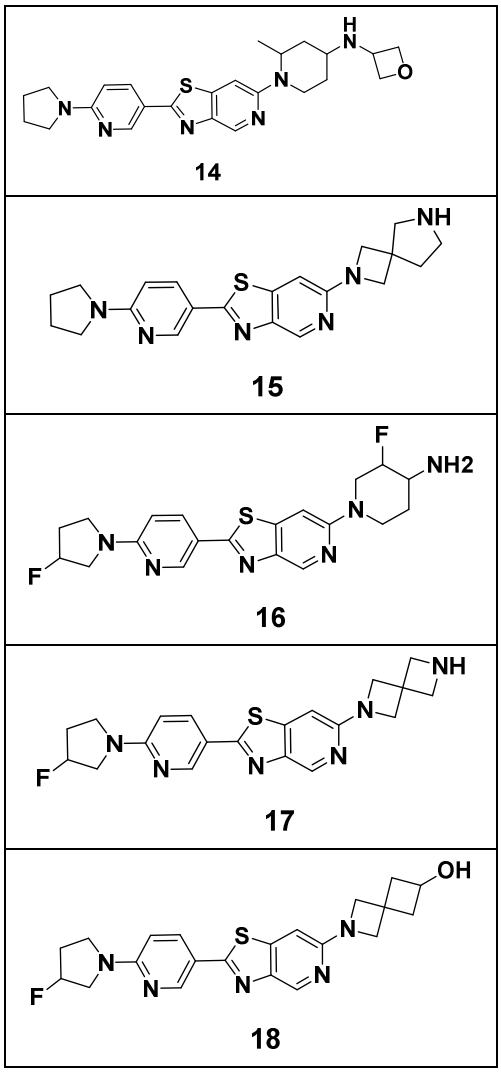
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6



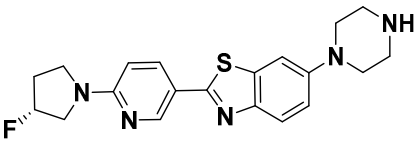
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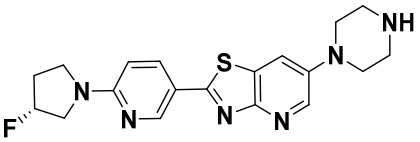


or a stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof.

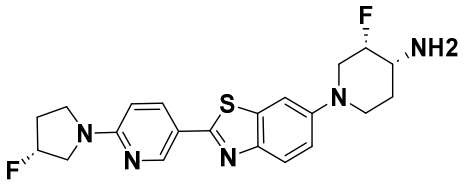
14. The compound according to claim 1, wherein the compound is selected from:



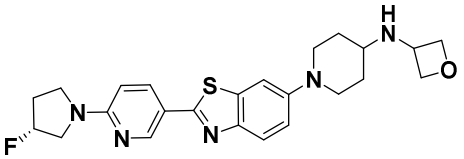
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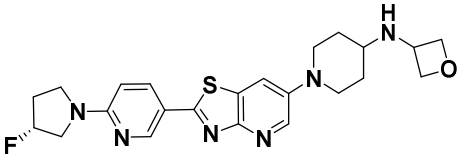
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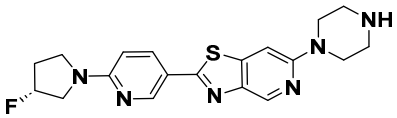
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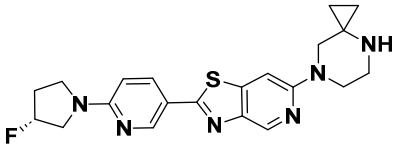
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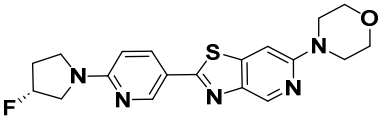
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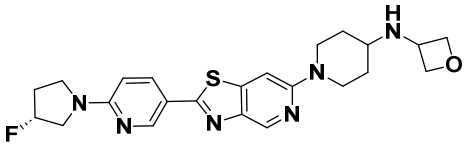
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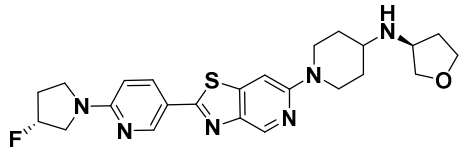
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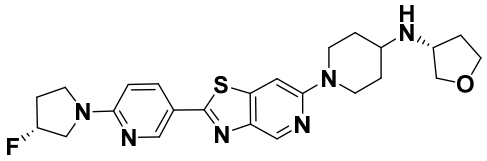
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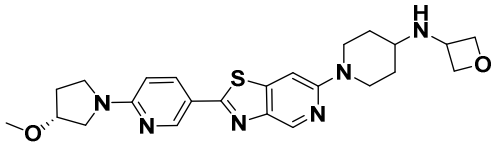
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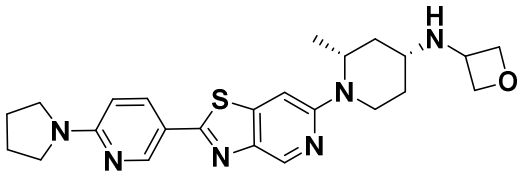
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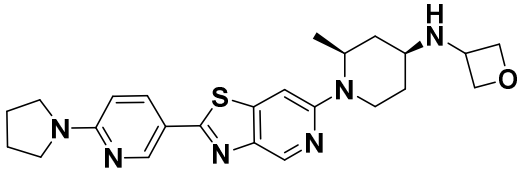
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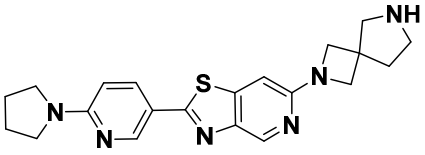
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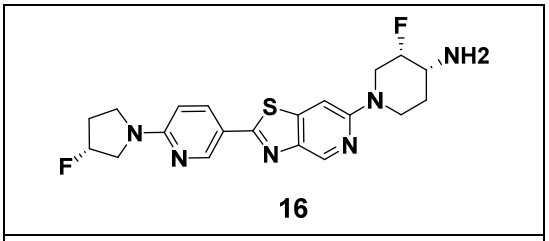
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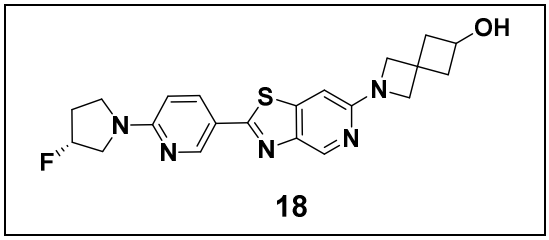
14



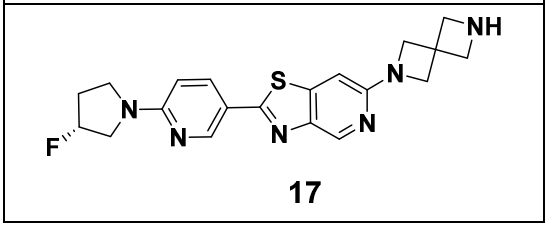
15



16



18



17

or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

15. A pharmaceutical composition comprising a compound according to any one of claims 1 to 14, and optionally at least one pharmaceutically acceptable excipient, carrier, diluent and/or adjuvant.

16. Use of the compound according to any one of claims 1 to 14, or the pharmaceutical composition according to claim 15, in the manufacture of a medicament for the prevention, alleviation or treatment of a disease, disorder or abnormality associated with alpha-synuclein aggregates.

17. The use according to claim 16, wherein the disease, disorder or abnormality is selected from Parkinson's disease (including sporadic, familial with alpha-synuclein mutations, familial with mutations other than alpha-synuclein, pure autonomic failure or Lewy body dysphagia), SNCA duplication carrier, Lewy Body dementia (LBD), dementia with Lewy bodies (DLB) (including “pure” Lewy body dementia), Parkinson’s disease dementia (PDD), diffuse Lewy body disease (DLBD), Alzheimer’s disease, sporadic Alzheimer’s disease, familial Alzheimer's disease with APP mutations, familial Alzheimer's disease with PS-1, PS-2 or other mutations, familial British dementia, Lewy body variant of Alzheimer’s disease, Down syndrome, multiple system atrophy (MSA) (including Shy-Drager syndrome, striatonigral degeneration or olivopontocerebellar atrophy), traumatic brain injury, chronic traumatic encephalopathy, dementia puglistica, tauopathies (including Pick's disease, frontotemporal dementia, progressive supranuclear palsy, corticobasal degeneration, Niemann-Pick type C1 disease, frontotemporal dementia with Parkinsonism linked to chromosome 17), Creutzfeldt-Jakob disease, Huntington's disease, motor neuron disease, amyotrophic lateral sclerosis (including sporadic, familial or ALS-dementia complex of Guam), neuroaxonal dystrophy, neurodegeneration with brain iron accumulation type 1 (including Hallervorden-Spatz syndrome), prion diseases, ataxia

telangiectatica, Meige's syndrome, subacute sclerosing panencephalitis, Gerstmann-Straussler-Scheinker disease, inclusion-body myositis, Gaucher disease, Krabbe disease as well as other lysosomal storage disorders (including Kufor-Rakeb syndrome and Sanfilippo syndrome) and rapid eye movement (REM) sleep behavior disorder.

18. The use according to claim 17, wherein the disease is Parkinson's disease.

19. The use according to claim 17, wherein the disease is multiple system atrophy.

20. The use according to claim 17, wherein the disease is dementia with Lewy bodies.

21. The use according to claim 17, wherein the disease is Parkinson's disease dementia.

22. The use according to claim 17, wherein the disease is SNCA duplication carrier.

23. The use according to claim 17, wherein the disease is Alzheimer's disease.

24. The use according to any one of claims 16 to 23, wherein the use is in a human.

25. Use of the compound according to any one of claims 1 to 14, in the manufacture of a medicament for inhibiting or preventing alpha-synuclein aggregation.

26. Use of the compound according to any one of claims 1 to 14, in the manufacture of a medicament for reducing the concentration of alpha-synuclein aggregates.

27. Use of the compound according to any one of claims 1 to 14, in the manufacture of a medicament for inhibiting *de novo* alpha-synuclein aggregate formation.

28. Use of the compound according to any one of claims 1 to 14as an *in vitro* analytical reference or an *in vitro* screening tool.

29. A mixture or a combination comprising a compound according to claims 1 to 14, and one or more therapeutic agent(s) different from the compound as defined in any one of claims 1 to 14, and optionally a pharmaceutically acceptable carrier, diluent, adjuvant and/or excipient.