3(4):565-7; Neal et al., Mol. Imaging Biol. 2013, 15:585-595; Bagchi et al., PLoS One 2013, 8(2):e55031; Yu et al., Bioorganic and Medicinal chemistry 2012, 20:4625-4634; Zhang et al., Appl Sci (Basel) 2014, 4(1):66-78; Chu et al., J. Med. Chem., 2015, 58 (15):6002-17).

WO 2011/128455 refers to specific compounds which are suitable for treating disorders associated with amyloid proteins or amyloid-like proteins. US 2012/0302755 relates to certain imaging agents for detecting neurological dysfunction. Further compounds for the diagnosis of neurodegenerative disorders on the olfactory epithelium are discussed in WO 2012/037928.

WO 2010/063701 refers to a certain *in vivo* imaging agent for use in a method to determine the presence of, or susceptibility to, Parkinson's disease, wherein the *in vivo* imaging agent comprises an alpha-synuclein binder labelled with an *in vivo* imaging moiety, and wherein the *in vivo* imaging agent binds to alpha-synuclein with a binding affinity.

US 2014/0142089 relates to a method for preventing or treating a degenerative brain disease, the method comprising administering to a subject in need thereof an effective amount of a pharmaceutical composition comprising a specific compound, a pharmaceutically acceptable salt, an isomer, a solvate, a hydrate, and a combination thereof.

WO 2009/155017 describes aryl or heteroaryl substituted azabenzoxazole derivatives, which are stated to be useful as tracers in positron emission tomography (PET) imaging to study amyloid deposits in the brain *in vivo* to allow diagnosis of Alzheimer's disease.

WO 2016/033445 refers to a specific compound for imaging huntingtin protein.

WO 2017/153601 and WO 2019/234243 refer to bicyclic compounds for diagnosing alpha-synuclein aggregates.

Therefore, there is a need for a new class of imaging compounds that bind with high affinity to alpha-synuclein.

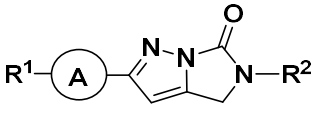
SUMMARY

The present disclosure provides compounds that can be employed in diagnosing a disease, disorder or abnormality associated with alpha-synuclein aggregates, including, but not limited to, Lewy bodies

and/or Lewy neurites (such as Parkinson's disease), prognosing such a disease, disorder or abnormality, and monitoring the progression of such a disease, disorder or abnormality. In particular, the compounds should be suitable for determining a predisposition to such a disease, disorder or abnormality, monitoring the progression of the disease, disorder or abnormality, or predicting the responsiveness of a patient who is suffering from such a disease, disorder or abnormality to the treatment with a certain medicament. Furthermore, the compounds should be suitable for diagnosing a disease, disorder or abnormality associated with alpha-synuclein aggregates and / or detecting and optionally quantifying alpha-synuclein aggregates.

Various examples of the disclosure are described herein.

In one aspect, provided herein is a compound of formula (I):


(I)

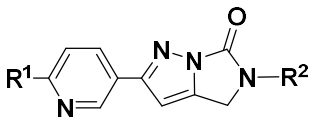
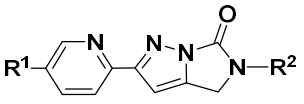
or a detectably labelled compound, stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein

Ⓐ is a 6-membered heteroaryl, which is optionally substituted with at least one substituent independently selected from halo, or C_1-C_4alkyl;

R^1 is halo, haloC_1-C_4alkoxy, or a 4- to 6-membered heterocyclyl which is optionally substituted with at least one halo; and

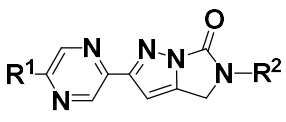
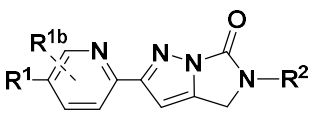
R^2 is a 5-membered or 6-membered heteroaryl optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl.

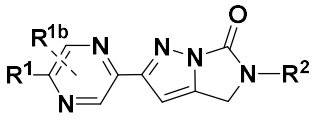
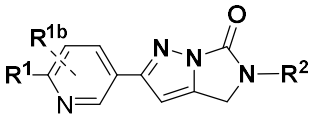
The disclosure is also directed to a compound having the following subformulae


(IIa), or 
(IIb)

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

The disclosure is also directed to a compound having the following subformulae


(IIb'), or 
(IIc) or


(IId), or 
(IIe)

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

In another aspect, the present disclosure provides a diagnostic composition comprising a compound of formula (I) as defined herein, and optionally at least one pharmaceutically acceptable excipient, carrier, diluent and/or adjuvant.

the present disclosure provides a compound of formula (I), or a diagnostic composition as defined herein, which can be use in the imaging of alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites. The compound of formula (I), or the diagnostic composition can be for use in positron emission tomography imaging of alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites. The compound of formula (I) or the diagnostic composition, as defined herein, can be for use for in vitro imaging, ex vivo imaging, or in vivo imaging, preferably the use is for in vivo imaging, more preferably the use is for brain imaging. The compound of formula (I) or the diagnostic composition, as defined herein, can be use in diagnostics.

In another aspect, the present disclosure provides a compound as defined herein, or a diagnostic composition as defined herein, for use in the imaging of alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites; or for use in positron emission tomography imaging of alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites.

In another aspect, the present disclosure provides a compound as defined herein, or a diagnostic composition as defined herein, for use in diagnostics, wherein the diagnostics are preferably the diagnostics of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites or a predisposition therefor, wherein the disease, disorder or abnormality is optionally 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 aspect, the present disclosure provides use of a compound as defined herein, or a diagnostic composition as defined herein for diagnostics, wherein the diagnostics are preferably the diagnostics of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites or a predisposition therefor, wherein the disease, disorder or abnormality is optionally 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.

The present disclosure refers to a method of diagnosing a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites, in a subject, the method comprising the steps:

(a) Administering a compound of formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein, to the subject;

(b) Allowing the compound to bind to the alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites; and

(c) Detecting the compound bound to the alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites.

The present disclosure refers to a method of positron emission tomography (PET) imaging of alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites, in a tissue of a subject, the method comprising the steps:

(a) Administering a compound of formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein to the subject;
(b) Allowing the compound to bind to the alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites; and
(c) Detecting the compound bound to the alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites by collecting a positron emission tomography (PET) image of the tissue of the subject.

The present disclosure is directed to a method for the detection and optionally quantification of alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites, in a tissue of a subject, the method comprising the steps:
(a) Bringing a sample or a specific body part or body area suspected to contain alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites, into contact with a compound of formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein;
(b) Allowing the compound to bind to the alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites;
(c) Detecting the compound bound to the alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites; and
(d) Optionally quantifying the amount of the compound bound to the alpha-synuclein aggregates, including, but not limited to, Lewy bodies and/or Lewy neurites.

The present disclosure is also directed to a method of collecting data for the diagnosis of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites, wherein the method comprises the steps:
(a) Bringing a sample or a specific body part or body area suspected to contain alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites into contact with a compound of the formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein;
(b) Allowing the compound to bind to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;
(c) Detecting the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites; and

(d) Optionally correlating the presence or absence of the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites with the presence or absence of the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in the sample or specific body part or body area.

The present disclosure also refers to a method of collecting data for determining a predisposition to a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites, the method comprising the steps:

(a) Bringing a sample or a specific body part or body area suspected to contain alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites into contact with a compound of the formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein;

(b) Allowing the compound to bind to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;

(c) Detecting the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites; and

(d) Optionally correlating the presence or absence of the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites with the presence or absence of the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in the sample or specific body part or body area.

The present disclosure also relates to a method of collecting data for prognosing a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites, wherein the method comprises the steps:

(a) Bringing a sample, a specific body part or body area suspected to contain alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites into contact with a compound of the formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein;

(b) Allowing the compound to bind to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;

(c) Detecting the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;

(d) Optionally correlating the presence or absence of the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites with the presence

or absence of the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in the sample or specific body part or body area; and

(e) Optionally repeating steps (a) to (c) and, if present, optional step (d) at least one time.

The present disclosure is directed to a method of collecting data for monitoring the progression of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in a patient, the method comprising the steps:

(a) Bringing a sample, a specific body part or body area suspected to contain alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites into contact with the compound of the formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein;

(b) Allowing the compound to bind to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;

(c) Detecting the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;

(d) Optionally correlating the presence or absence of the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites with the presence or absence of the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in the sample or specific body part or body area; and

(e) Optionally repeating steps (a) to (c) and, if present, optional step (d) at least one time.

The present disclosure relates to a method of collecting data for predicting responsiveness of a patient suffering from a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites to a medicament, the method comprising the steps:

(a) Bringing a sample, a specific body part or body area suspected to contain alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites into contact with a compound of formula (I), or a diagnostic composition which comprises a compound of formula (I), as defined herein;

(b) Allowing the compound to bind to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;

(c) Detecting the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites;

(d) Optionally correlating the presence or absence of the compound bound to the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites with the presence or absence of the alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in the sample or specific body part or body area; and

(e) Optionally repeating steps (a) to (c) and, if present, optional step (d) at least one time.

In another aspect, the present disclosure is directed to a method comprising the steps:

(a) Bringing a sample suspected to contain an alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites, into contact with a compound as defined herein, or a diagnostic composition as defined herein which comprises a compound as defined herein;

(b) Allowing the compound to bind to the alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites;

(c) Detecting the compound bound to the alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites using positron emission tomography; and

wherein the method is selected from:

(i) a method for the detection and optionally quantification of alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites, in a tissue of a subject,

(ii) a method of collecting data for the diagnosis of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites,

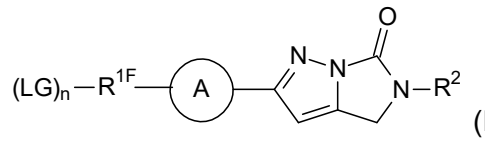
(iii) a method of collecting data for determining a predisposition to a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites,

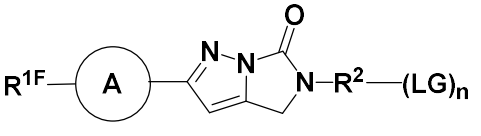
(iv) a method of collecting data for prognosing a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites,

(v) a method of collecting data for monitoring the progression of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in a patient, or

(vi) a method of collecting data for predicting responsiveness of a patient suffering from a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites to a treatment with a medicament.

The disclosure is further directed to a compound of formula (III-F) or (III-F´):


(III-F)


(III-F')

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

Ⓐ is a 6-membered heteroaryl which is optionally substituted with at least one substituent independently selected from halo, or C_1-C_4alkyl

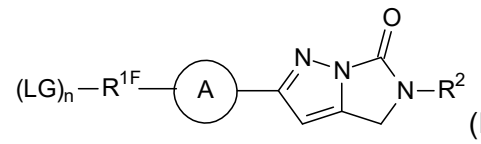
R^{1F} is a 4- to 6-membered heterocyclyl, or C_1-C_4alkoxy;

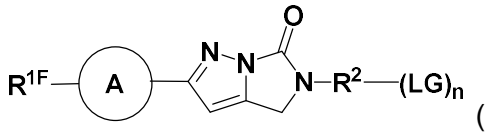
R^2 is a 5-membered or 6-membered heteroaryl optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl;

LG is a leaving group; and

n is at least 1.

In another aspect, the disclosure is further directed to a compound of formula (III-F) or (III-F´)


(III-F)


(III-F')

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

Ⓐ is a 6-membered heteroaryl; which is optionally substituted with at least one substituent independently selected from halo, or C_1-C_4alkyl

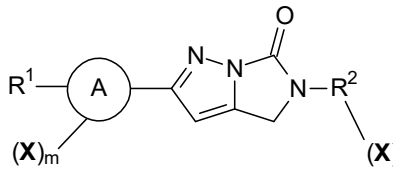
R^{1F} is a 4- to 6-membered heterocyclyl or C_1-C_4alkoxy;

R^2 is a 5-membered or 6-membered heteroaryl optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl;

LG is a leaving group, which is preferably selected from bromo, chloro, iodo, C_1–C_4alkylsulfonate and C_6–C_{10}arylsulfonate, wherein the C_6–C_{10}arylsulfonate can be optionally substituted with $–CH_3$ or $–NO_2$; and

n is at least 1.

In another aspect the disclosure is further directed to a compound of formula (III-H)



(III-H)

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

Ⓐ is a 6-membered heteroaryl, which is optionally substituted with at least one substituent independently selected from halo, or C_1-C_4alkyl;

R^1 is halo or a 4- to 6-membered heterocyclyl which is optionally substituted with at least one halo or haloC_1-C_4alkoxy;

R^2 is a 5-membered or 6-membered heteroaryl, optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl;

m is 0, 1, or 2;

p is 0, 1, or 2; and

X is bromo, chloro or iodo;

with the proviso that the compound of formula (III-H) comprises at least one **X**.

The disclosure is further directed to a method of preparing a compound of formula (I-F), by reacting a compound of formula (III-F) with a ^{18}F-fluorinating agent, so that the Leaving Group (LG) is replaced by ^{18}F. In another aspect, the disclosure is further directed to a method of preparing the compound as defined herein comprising reacting the compound of formula (III-F) or (III-F´) as defined herein with a ^{18}F-fluorinating agent, so that LG is replaced by ^{18}F, wherein the ^{18}F-fluorinating agent is preferably selected from K^{18}F, Rb^{18}F, Cs^{18}F, Na^{18}F, Kryptofix[222]K^{18}F, tetra(C_{1-6}alkyl)ammonium salt of ^{18}F, and tetrabutylammonium [^{18}F]fluoride.

The disclosure is further directed to a method of preparing a compound of formula (I-H), by reacting the compound of formula (III-H) with a ^{3}H radiolabelling agent, so that X is replaced by ^{3}H. In another aspect, the disclosure is further directed to a method of preparing the compound as defined herein, comprising reacting the compound of formula (III-H) as defined herein with a ^{3}H radiolabelling agent.

The disclosure is further directed to the use of the compound according to compound of formula (I) as an *in vitro* analytical reference or an *in vitro* screening tool. In another aspect, the present disclosure provides a compound as defined herein, for use as an *in vitro* analytical reference or an *in vitro* screening tool.

In another aspect, the disclosure is further directed to a test kit for detection and/or diagnosis of a disease, disorder or abnormality associated with alpha-synuclein aggregates, wherein the test kit comprises at least one compound of formula (I) as defined herein.

The disclosure is further directed to a kit for preparing a radiopharmaceutical preparation, wherein the kit comprises a sealed vial containing at least one compound of formula (III-F) or (III-H). In another

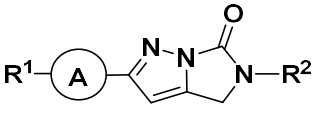
aspect, the disclosure is further directed to a kit for preparing a radiopharmaceutical preparation, wherein the kit comprises a sealed vial containing at least one compound as defined herein.

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.

CLAIMS

1. A compound of formula (I):


(I)

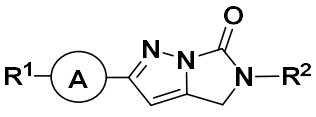
or a detectably labelled compound, stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein

Ⓐ is a 6-membered heteroaryl which is optionally substituted with at least one substituent independently selected from halo, or C_1-C_4alkyl;

R^1 is halo, haloC_1-C_4alkoxy, or a 4- to 6-membered heterocyclyl which is optionally substituted with at least one halo; and

R^2 is a 5-membered or 6-membered heteroaryl optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl.

2. The compound of formula (I) according to claim 1:


(I)

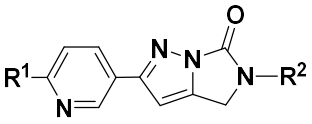
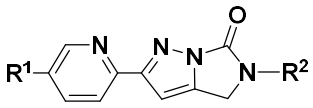
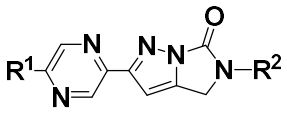
or a detectably labelled compound, stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein

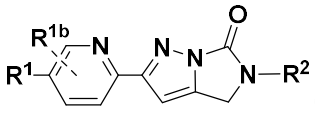
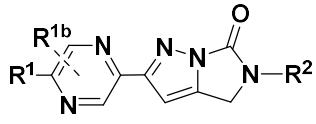
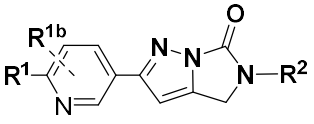
Ⓐ is a 6-membered heteroaryl;

R^1 is halo, or a 4- to 6-membered heterocyclyl which is optionally substituted with at least one halo; and

R^2 is a 5-membered or 6-membered heteroaryl optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl.

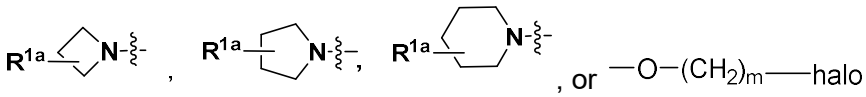
3. The compound according to claim 1 or 2, having a formula (IIa), (IIb), (IIb'), (IIc), (IId) or (IIe):


(IIa), or

(IIb), or

(IIb'), or


(IIc) or

(IId), or

(IIe)

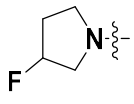
or a detectably labelled compound, stereoisomer, racemic mixture, pharmaceutically acceptable salt, hydrate, or solvate thereof, wherein R^{1b} is halo or C_1-C_4alkyl.

4. The compound according to any one of claims 1 to 3, wherein **R^1** is a 4- to 6-membered heterocyclyl selected from the following:

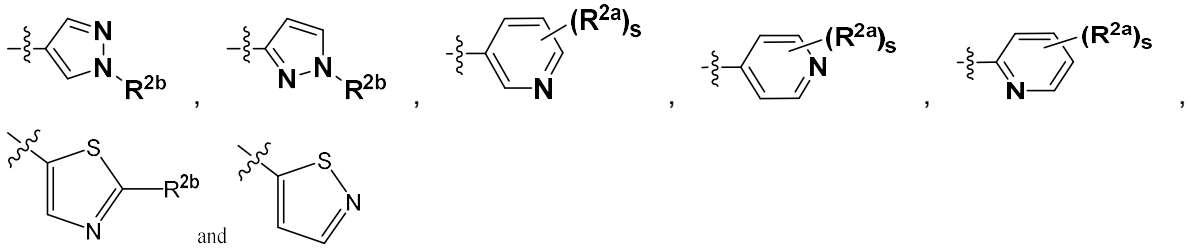


wherein R^{1a} is halo or H, and m is 1 or 2;

wherein **R^1** is preferably a 5-membered heterocyclyl selected from the following:



5. The compound according to any one of claims 1 to 4, wherein **R^2** is a 5-membered or 6-membered heteroaryl selected from the following:

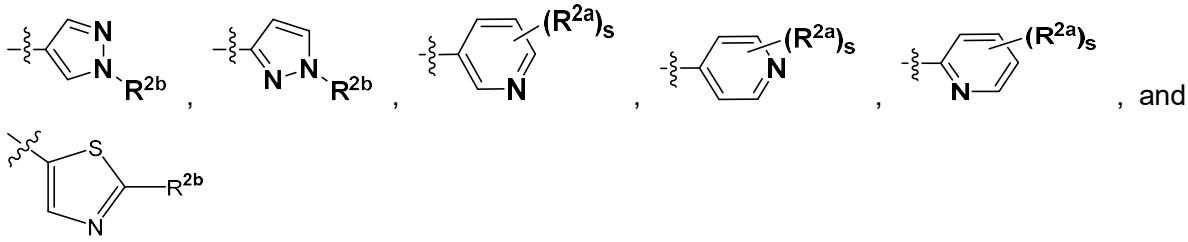


wherein

R^{2a} is independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl;

R^{2b} is selected from H, haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl; and

s is 0, 1 or 2; wherein **R^2** is preferably a 5-membered or 6-membered heteroaryl selected from the following:

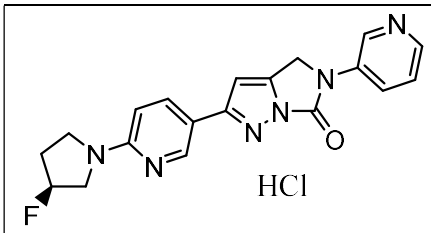


wherein

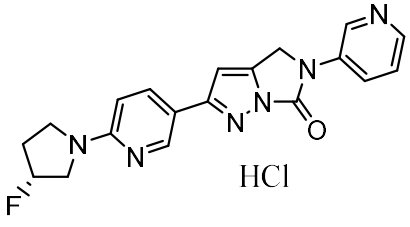
R^{2b} is selected from H, C_1-C_4alkyl, and haloC_1-C_4alkyl; and

s is 0.

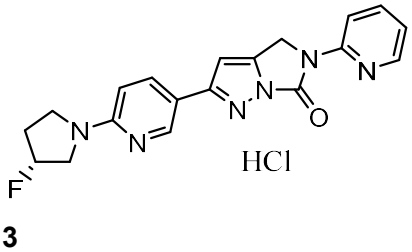
6. The compound according to claim 1, wherein the compound is selected from:



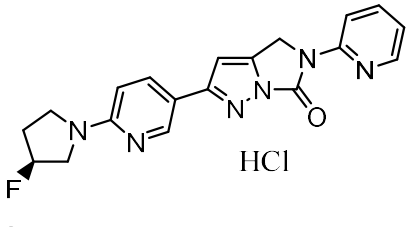
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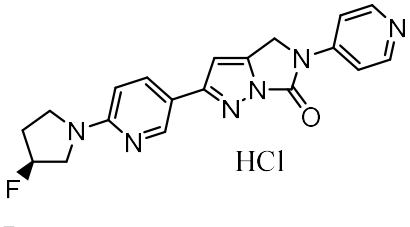
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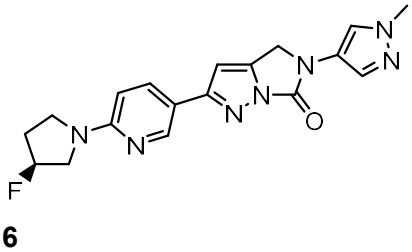
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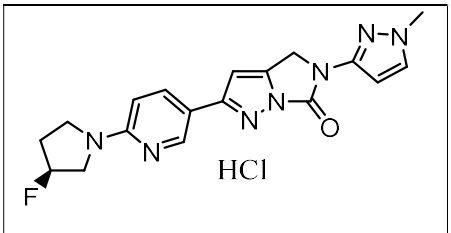
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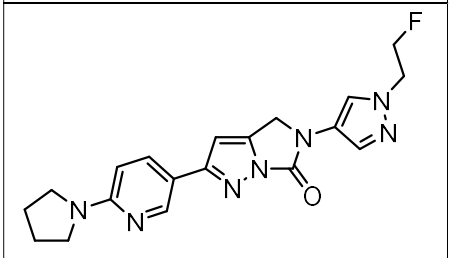
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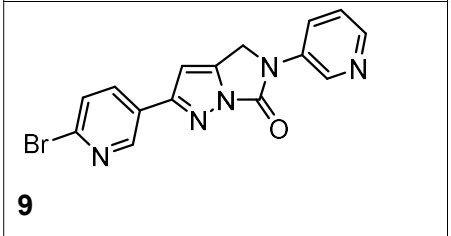
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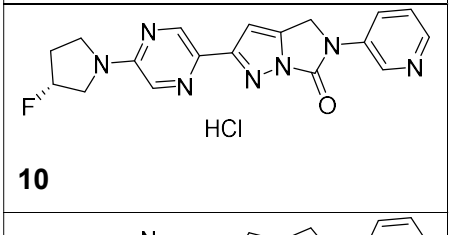
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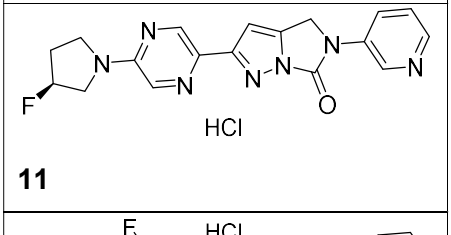
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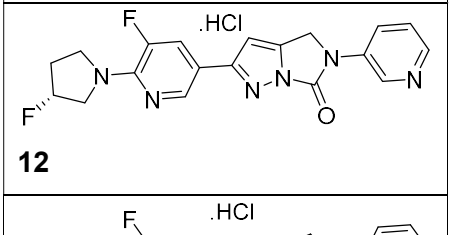
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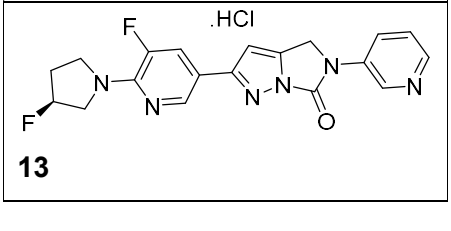
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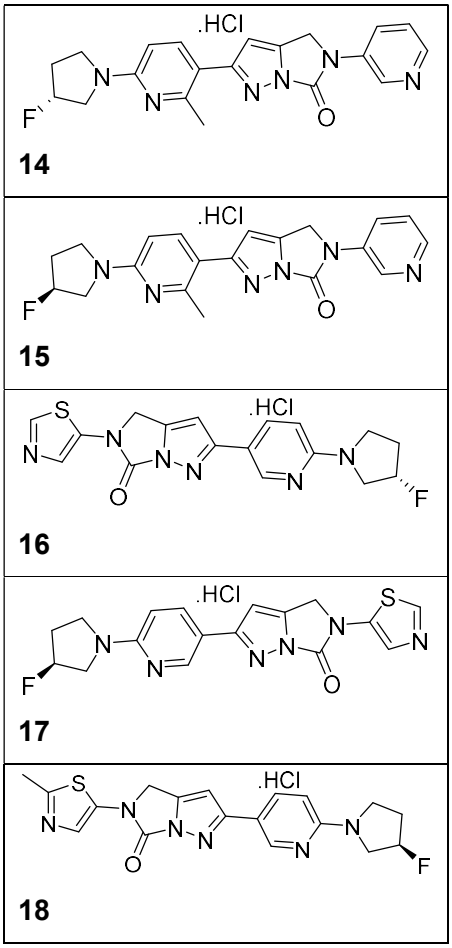
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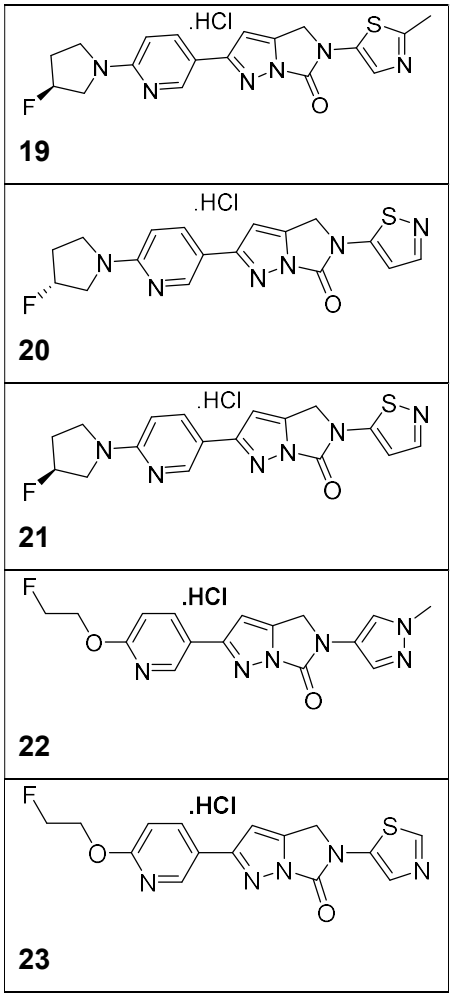


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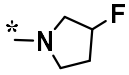
13





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

7. The compound according to any one of the preceding claims, wherein the compound is a detectably labelled compound; wherein the detectable label is preferably selected from a radioisotope, preferably ^{2}H, ^{3}H or ^{18}F .

8. The compound according to claim 7 wherein R^1 is  and the compound of formula (I) is detectably labelled at least at one available position by ^{3}H.

9. A diagnostic composition comprising a compound according to any one of claims 1 to 8, and optionally at least one pharmaceutically acceptable excipient, carrier, diluent and/or adjuvant.

10. A compound according to claim 7 or 8, or a diagnostic composition according to claim 9, for use in the imaging of alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites; or for use in positron emission tomography imaging of alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites.

11. The compound for use or the diagnostic composition for use according to claim 10, wherein the use is for *in vitro* imaging, *ex vivo* imaging, or *in vivo* imaging, preferably the use is for *in vivo* imaging, more preferably the use is for brain imaging.

12. A compound according to claim 7 or 8, or a diagnostic composition according to claim 9, for use in diagnostics, wherein the diagnostics are preferably the diagnostics of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites or a predisposition therefor, wherein the disease, disorder or abnormality is optionally 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.

13. Use of a compound according to claim 7 or 8, or a diagnostic composition according to claim 9 for diagnostics, wherein the diagnostics are preferably the diagnostics of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites or a predisposition therefor, wherein the disease, disorder or abnormality is optionally 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.

14. The compound for use or the diagnostic composition for use according to claim 12, or the use according to claim 13, wherein the disease is Parkinson's disease, multiple system atrophy, dementia with Lewy bodies, Parkinson’s disease dementia, SNCA duplication carrier or Alzheimer’s disease.

15. A method comprising the steps:

(a) Bringing a sample suspected to contain an alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites, into contact with a compound according to any one of claims 1 to 8, or a diagnostic composition according to claim 9 which comprises a compound according to any one of claims 1 to 8;

(b) Allowing the compound to bind to the alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites;

(c) Detecting the compound bound to the alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites using positron emission tomography; and

wherein the method is selected from:

(i) a method for the detection and optionally quantification of alpha-synuclein aggregates, including but not limited to, Lewy bodies and/or Lewy neurites, in a tissue of a subject,

(ii) a method of collecting data for the diagnosis of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites,

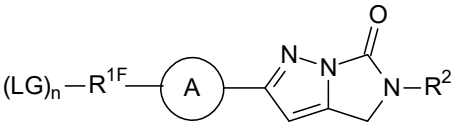
(iii) a method of collecting data for determining a predisposition to a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites,

(iv) a method of collecting data for prognosing a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites,

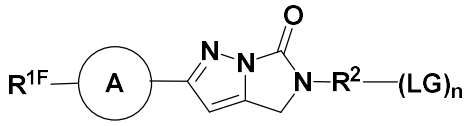
(v) a method of collecting data for monitoring the progression of a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites in a patient, or

(vi) a method of collecting data for predicting responsiveness of a patient suffering from a disease, disorder or abnormality associated with alpha-synuclein aggregates including, but not limited to, Lewy bodies and/or Lewy neurites to a treatment with a medicament.

16. A compound of formula (III-F) or (III-F´)



(III-F)



(III-F')

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

Ⓐ is a 6-membered heteroaryl; which is optionally substituted with at least one substituent independently selected from halo, or C_1-C_4alkyl

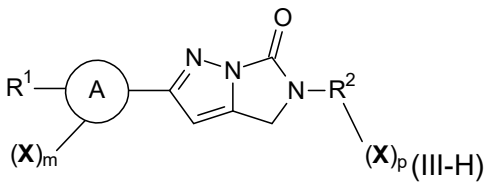
R^{1F} is a 4- to 6-membered heterocyclyl or C_1-C_4alkoxy;

R^2 is a 5-membered or 6-membered heteroaryl optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl;

LG is a leaving group, which is preferably selected from bromo, chloro, iodo, C_1–C_4alkylsulfonate and C_6–C_{10}arylsulfonate, wherein the C_6–C_{10}arylsulfonate can be optionally substituted with $–CH_3$ or $–NO_2$; and

n is at least 1.

17. A compound of formula (III-H)



(III-H)

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

Ⓐ is a 6-membered heteroaryl which is optionally substituted with at least one substituent independently selected from halo, or C_1-C_4alkyl;

R^1 is halo or a 4- to 6-membered heterocyclyl which is optionally substituted with at least one halo, or haloC_1-C_4alkoxy;

R^2 is a 5-membered or 6-membered heteroaryl, optionally substituted with 1 or 2 substituents independently selected from haloC_1-C_4alkyl, haloC_1-C_4alkoxy, C_1-C_4alkoxy, and C_1-C_4alkyl;

m is 0, 1, or 2;

p is 0, 1, or 2; and

X is bromo, chloro or iodo;

with the proviso that the compound of formula (III-H) comprises at least one **X**.

18. A method of preparing the compound according to claim 7 comprising reacting the compound of formula (III-F) or (III-F´) according to claim 16 with a ^{18}F-fluorinating agent, so that LG is replaced by ^{18}F, wherein the ^{18}F-fluorinating agent is preferably selected from K^{18}F, Rb^{18}F, Cs^{18}F, Na^{18}F, Kryptofix[222]K^{18}F, tetra(C_{1-6}alkyl)ammonium salt of ^{18}F, and tetrabutylammonium [^{18}F]fluoride.

19. A method of preparing the compound according to claim 7, comprising reacting the compound of formula (III-H) according to claim 17 with a ^{3}H radiolabelling agent.

20. A compound according to any one of claims 1 to 8, for use as an *in vitro* analytical reference or an *in vitro* screening tool.

21. A test kit for the detection and/or diagnosis of a disease, disorder or abnormality associated with alpha-synuclein aggregates, wherein the test kit comprises at least one compound as defined in any one of claims 1 to 8.

22. A kit for preparing a radiopharmaceutical preparation, wherein the kit comprises a sealed vial containing at least one compound as defined in claim 16 or 17.