Mutations in the gene encoding glucocerebrosidase are also a risk factor for α-synucleinopathies, such as Parkinson's disease and diffuse Lewy Body disease. Parkinson's disease is a degenerative disorder of the central nervous system associated with death of dopamine-containing cells in a region of the midbrain. Diffuse Lewy Body disease is a dementia that is sometimes confused with Alzheimer's disease.

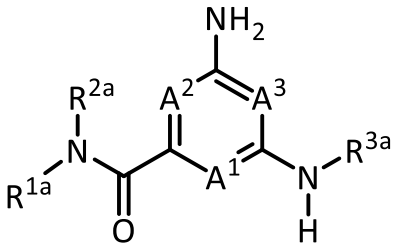
Small molecules capable of binding allosterically or competitively to mutated β-glucocerebrosidase enzyme, thereby stabilizing the enzyme against degradation (chaperones), constitute an important therapeutic target in conditions associated with the alteration of the activity of β-glucocerebrosidase. By binding and stabilizing mutant proteins, these chemical chaperones facilitate protein folding and eventually increase their transport to the lysosome. Improved trafficking of the mutant protein from the ER to the lysosome results in the reduction of lysosome size and correction of the storage. These chaperones may also increase the stability of mutant enzymes toward degradation in the lysosome. *See, e.g.,* Patniak *et al., Journal of Medicinal Chemistry* 55(12):5734-5748 (2012).

It has been surprisingly found that compounds of formulae (IA) and (IB) are capable of binding to β-glucocerebrosidase thereby stabilizing the enzyme against denaturation.

BRIEF SUMMARY OF THE DISCLOSURE

The present disclosure is related to the discovery that heteroaryl compounds represented by formulae (IA) and (IB) are capable of binding to β-glucocerebrosidase (mutated or not) and are thus useful in the treatment or prevention of, e.g., a lysosomal storage disease, such as Gaucher's disease, or α-synucleinopathies, such as Parkinson's disease, or other conditions associated with the alteration of the activity of β-glucocerebrosidase.

In a first aspect, the present disclosure refers to a compound of formula (IA):



(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N and no more than two of A^1, A^2, or A^3 are N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N$(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

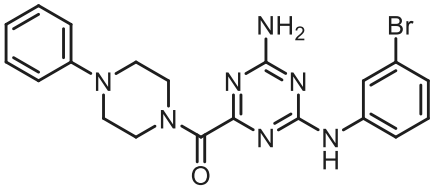
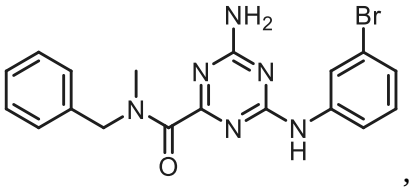
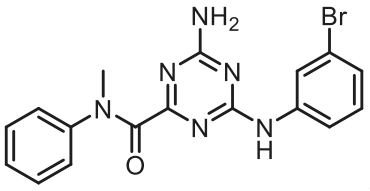
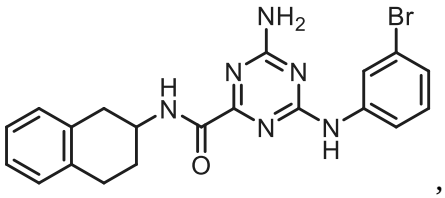
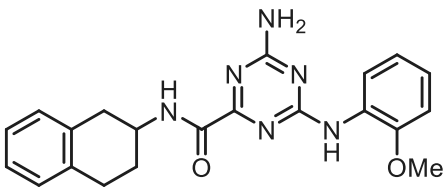
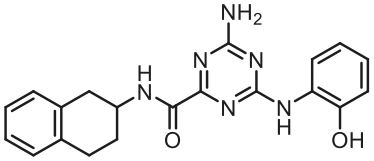
Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N$(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally

substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

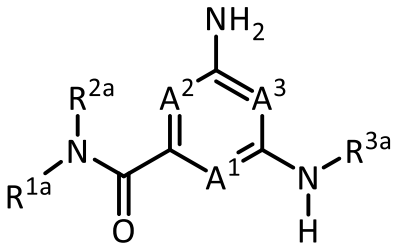
R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic.

In another aspect, the present disclosure refers to a compound, which is selected from the group consisting of


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or a pharmaceutically aceptable salt or solvate thereof.

In yet another aspect, the present disclosure refers to a pharmaceutical composition, comprising an effective amount of a compound of formula (IA):



(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N$(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9}

heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a,

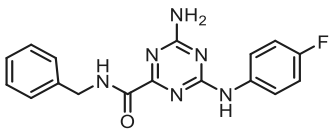
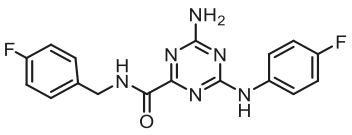
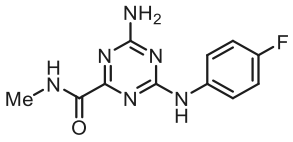
-$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

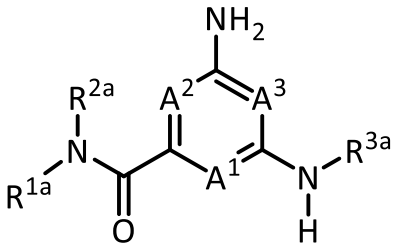
and at least one pharmaceutically acceptable excipient,

with the proviso that the compound is not


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In a further aspect, the present disclosure refers to a pharmaceutical composition, comprising a compound as disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

In another aspect, the present disclosure refers to a compound of formula (IA):



(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N$(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9}

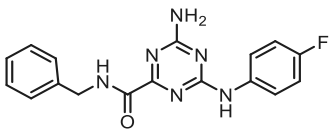
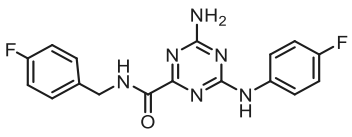
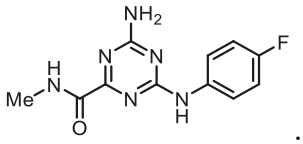
heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

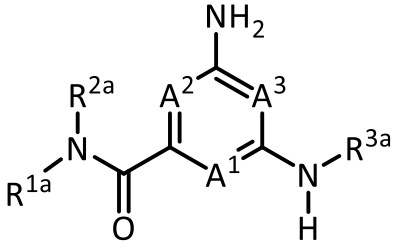
R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

for use as a medicament,

with the proviso that the compound is not


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, or 
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In yet another aspect, the present disclosure refers to a compound of formula (IA):


(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and C(R^{4a}), provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally

substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

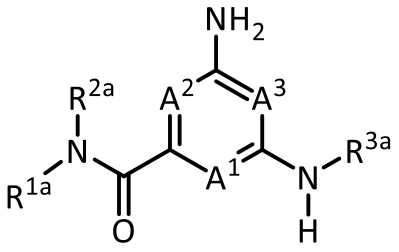
(a) for use in the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient;

(b) for use in the treatment or prevention of a lysosomal storage disease;

(c) for use in the treatment or prevention of an α-synucleinopathy; or

(d) for use in the treatment or prevention of a disease or disorder, wherein said disease or disorder is selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

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



(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N$(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9}

heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

(a) in the manufacture of a medicament for the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient;

(b) in the manufacture of a medicament for the treatment or prevention of a lysosomal storage disease;

(c) in the manufacture of a medicament for the treatment or prevention of an α-synucleinopathy; or

(d) in the manufacture of a medicament for the treatment or prevention of a disease or disorder selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an

anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

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

In yet another aspect, the present disclosure refers to a pharmaceutical composition as disclosed herein (a) for use in the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient; (b) for use in the treatment or prevention of a lysosomal storage disease; (c) for use in the treatment or prevention of an α-synucleinopathy; or (d) for use in the treatment or prevention of a disease or disorder, wherein said disease or disorder is selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

In a further aspect, the present disclosure refers to a use of a pharmaceutical composition as disclosed herein in the manufacture of a medicament (a) for use in the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient; (b) for use in the treatment or prevention of a lysosomal storage disease; (c) for use in the treatment or prevention of an α-synucleinopathy; or (d) for use in the treatment or prevention of a disease or disorder, wherein said disease or disorder is selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic

Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

In one example, the present disclosure provides compounds represented by formulae (IA) and (IB) below, and pharmaceutically acceptable salts and solvates thereof, collectively referred to herein as "Compounds of the Disclosure" (each is individually referred to hereinafter as a "Compound of the Disclosure").

In another example, the present disclosure provides a method of treating or preventing a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient in need thereof. The method comprises administering to the patient in need thereof an effective amount of a Compound of the Disclosure.

In another example, the present disclosure provides a method of treating or preventing a lysosomal storage disease, such as Gaucher’s disease, in a patient in need thereof by administering an effective amount of a Compound of the Disclosure.

In another example, the present disclosure provides a method of treating or preventing an α-synucleinopathy, such as Parkinson's disease, in a patient in need thereof by administering an effective amount of a Compound of the Disclosure.

In another example, the present disclosure is directed to a method of treating or preventing a disease or disorder selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

In another example, the methods described herein further comprise administering to the patient at least one other therapeutic agent. In another example, the therapeutic agent is an effective amount of an enzyme for enzyme replacement therapy. In another asoect, the enzyme is β-glucocerebrosidase or an analog thereof. In another example, the enzyme is imiglucerase. In another example, the therapeutic agent is an effective amount of a small molecule chaperone. In another example, the small molecule chaperone binds competitively to an enzyme. In another example, the small molecule chaperone is selected from the group consisting of iminoalditols, iminosugars, aminosugars, thiophenylglycosides, glycosidase, sulfatase, glycosyl transferase, phosphatase, and peptidase inhibitors. In another example, the small molecule chaperone is selected from the group consisting of isofagomine, N-nonyl-1-deoxynojirimycin (NN-DNJ), ambroxol, and miglustat. In another example, the small molecule chaperone is selected from the group consisting of isofagomine, N-nonyl-1-deoxynojirimycin (NN-DNJ), and ambroxol. In another example, the small molecule chaperone is miglustat.

In another example, the therapeutic agent is an effective amount of substrate reduction agent for substrate reduction therapy. In another example, the substrate reduction agent is miglustat.

In another example, the present disclosure provides a Compound of the Disclosure, as described herein, for use in the prevention or treatment of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient in need thereof.

In another example, the present disclosure provides a Compound of the Disclosure, as described herein, for use in the prevention or treatment of a lysosomal storage disease, such as Gaucher’s disease.

In another example, the present disclosure provides a Compound of the Disclosure, as described herein, for use in the prevention or treatment of an α-synucleinopathy, such as Parkinson's disease.

In another example, the present disclosure provides a Compound of the Disclosure, as described herein, for use in the prevention or treatment of a disease or disorder selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

In another example, the present disclosure is also directed to the use of a Compound of the Disclosure, as described herein, for the treatment or prevention of a a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient in need thereof, such as lysosomal storage diseases and α-synucleinopathies described herein.

In another example, the present disclosure provides a pharmaceutical composition comprising a Compound of the Disclosure, as described herein, and at least one pharmaceutically acceptable excipient.

In another example, the present disclosure provides a Compound of the Disclosure, as described herein, for use as a medicament.

In another example, the present disclosure provides use of a Compound of the Disclosure, as described herein, in the preparation of a medicament for the prevention or treatment of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient in need thereof, such as lysosomal storage diseases and α-synucleinopathies described herein.

In another example, the present disclosure provides a pharmaceutical composition comprising a Compound of the Disclosure, as described herein, and at least one pharmaceutically acceptable excipient, for use in the treatment or prevention of a a condition associated with the

alteration of the activity of β-glucocerebrosidase in a patient in need thereof, such as lysosomal storage diseases and α-synucleinopathies described herein.

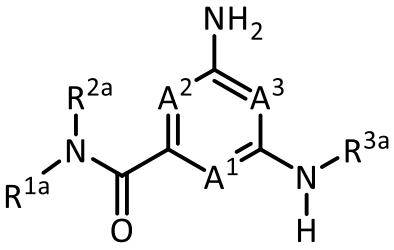
Other examples and advantages of the disclosure will be readily apparent from the following detailed description of the disclosure. The examples and advantages of the disclosure will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

It is to be understood that both the foregoing summary and the following detailed description are exemplary and explanatory only, and are not restrictive of the disclosure as claimed.

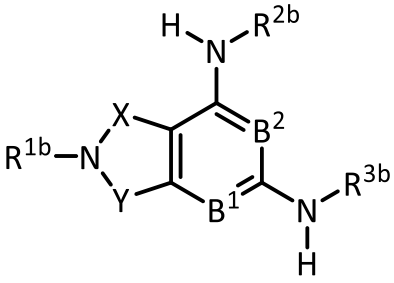
DETAILED DESCRIPTION OF THE DISCLOSURE

One aspect of the disclosure is based on the use of Compounds of the Disclosure for binding to β-glucocerebrosidase. In view of this property, Compounds of the Disclosure are expected to be useful for treating or preventing, e.g., Gaucher's disease and other diseases or conditions described herein.

Compounds of the Disclosure useful in this aspect of the disclosure are compounds of formula (IA) and formula (IB):



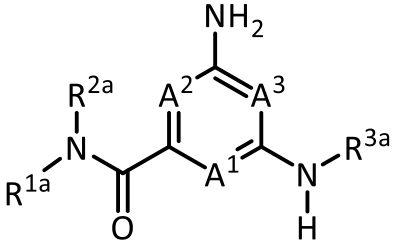
(IA) and



(IB),

and the pharmaceutically acceptable salts and solvates thereof, wherein A^1, A^2, A^3, R^{1a}, R^{2a}, R^{3a}, B^1, B^2, R^{1b}, R^{2b}, and R^{3b} are as defined below.

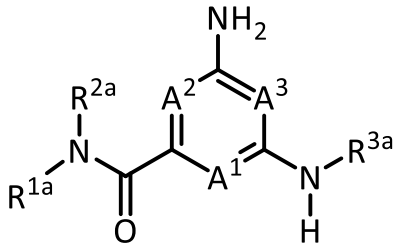
In another aspect, Compounds of the Disclosure are compounds of formula (IA):



(IA),

WHAT IS CLAIMED IS:

1. A compound of formula (IA):



(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N and no more than two of A^1, A^2, or A^3 are N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring

optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic.

2. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein A^1 is N and A^2 and A^3 are each independently selected from the group consisting of CH and $C(R^{4a})$.

3. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein (i) A^2 is N and A^1 and A^3 are each independently selected from the group consisting of CH and $C(R^{4a})$; (ii) A^3 is N and A^1 and A^2 are each independently selected from the group consisting of CH and $C(R^{4a})$; (iii) A^1 and A^2 are both N and A^3 is CH or $C(R^{4a})$; (iv) A^1 and A^3 are both N and A^2 is CH or $C(R^{4a})$; or (v) A^2 and A^3 are both N and A^1 is CH or $C(R^{4a})$.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{3a} is unsubstituted -C_{6-10} aryl or -C_{6-10} aryl substituted with 1 or 2 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -O(C_{1-4})alkyl, -S(C_{1-4})alkyl, -N(C_{1-4} alkyl)$_2$, -NH(C_{1-4} alkyl), and -C_{1-4} alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -O(C_{1-4})alkyl, -N(C_{1-4} alkyl)$_2$, and -NH(C_{1-4} alkyl).

5. The compound of claim 4, wherein R^{3a} is phenyl substituted with 1 or 2 substituents each independently selected from the group consisting of F, CL, Br, I, hydroxy, methyl, methoxy, and –CN.

6. The compound of claim 5, wherein R^{3a} is phenyl substituted with F or hydroxy at the ortho- or meta-position of the phenyl ring.

7. The compound of any one of claims 1-3, wherein R^{3a} is unsubstituted -C_{6-10} aryl fused to a 5- or 6-membered heterocyclic ring.

8. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{3a} is unsubstituted –(5- to 10-membered)-C_{6-9} heteroaryl or –(5- to 10-membered)-C_{6-9} heteroaryl substituted with 1 or 2 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -O(C_{1-4})alkyl, -S(C_{1-4})alkyl, -N(C_{1-4} alkyl)$_2$, -NH(C_{1-4} alkyl), and -C_{1-4} alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -O(C_{1-4})alkyl, -N(C_{1-4} alkyl)$_2$, and -NH(C_{1-4} alkyl).

9. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{3a} is unsubstituted –C_{3-10} cycloalkyl or -C_{3-10} cycloalkyl substituted with 1 or 2 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -O(C_{1-4})alkyl, -S(C_{1-4})alkyl, -N(C_{1-4} alkyl)$_2$, -NH(C_{1-4} alkyl), and -C_{1-4} alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -O(C_{1-4})alkyl, -N(C_{1-4} alkyl)$_2$, and -NH(C_{1-4} alkyl).

10. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{3a} is -(5- to 10-membered)-C_{2-9} heterocyclyl optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -N(Rb^a)$_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl.

11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{2a} is H.

12. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{2a} is -C_{1-4} alkyl.

13. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1a} is -C_{6-10} aryl or -C_{1-4} alkyl-C_{6-10} aryl, wherein said aryl or alkylaryl is optionally substituted with 1, 2 or 3 groups each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein Rb^a is as defined in claim 1; and wherein said aryl is optionally fused to a further (second) ring.

14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1a} is unsubstituted phenyl or unsubstituted benzyl.

15. The compound of any one of claims 1-13, wherein R^{1a} is phenyl fused to a 5- or 6-membered heterocyclic ring.

16. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1a} is $-C_{3-10}$ cycloalkyl or $-C_{1-4}$ alkyl-C_{3-10} cycloalkyl, wherein said cycloalkyl or alkylcycloalkyl is optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein Rb^a is as defined in claim 1; and wherein said cycloalkyl is optionally fused to a further (second) ring.

17. The compound of any one of claims 1-12 or 16, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1a} is unsubstituted $-C_{3-10}$ cycloalkyl fused to a phenyl ring.

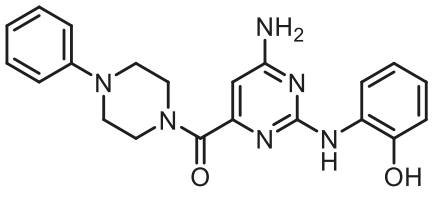
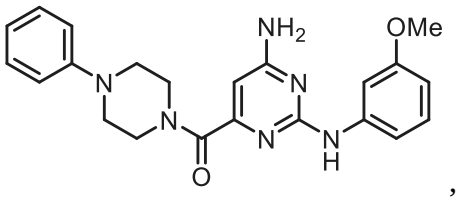
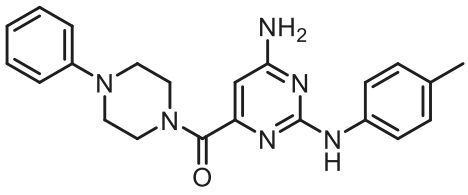
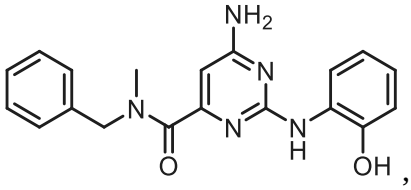
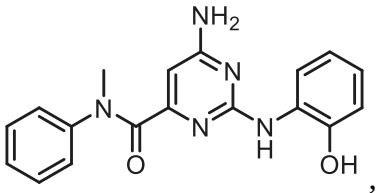
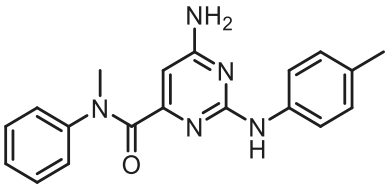
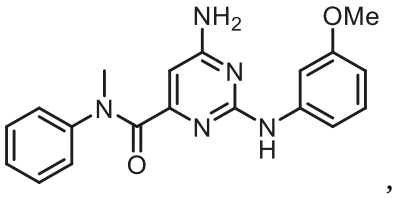
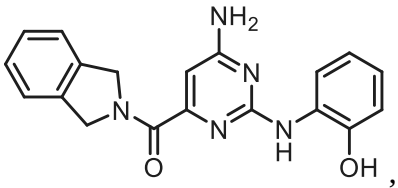
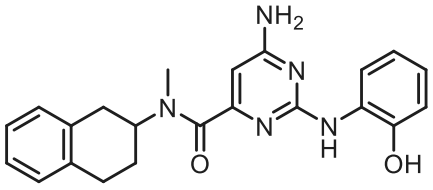
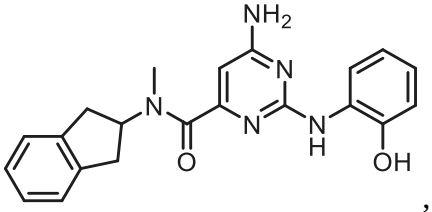
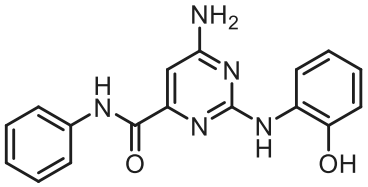
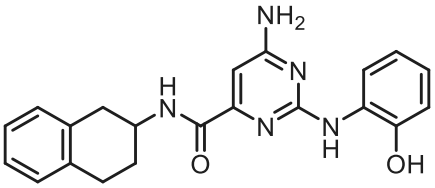
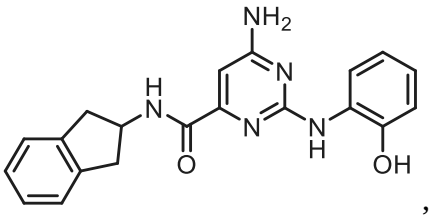
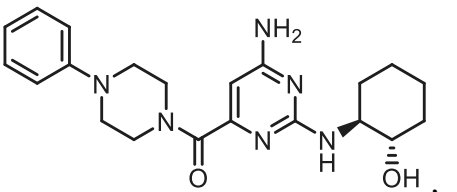
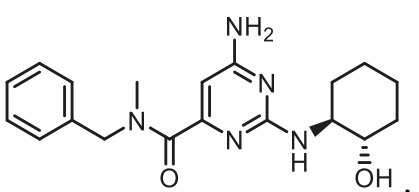
18. The compound of claim 17, wherein R^{1a} is $-C_{4-7}$ cycloalkyl fused to a phenyl ring.

19. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt or solvate thereof, wherein Rb^a is hydrogen or -C_{1-4} alkyl.

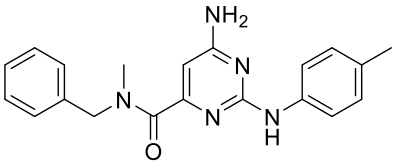
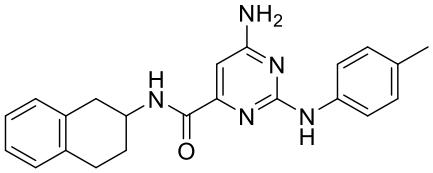
20. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring.

21. The compound of claim 20, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally fused to a phenyl ring.

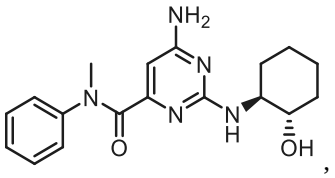
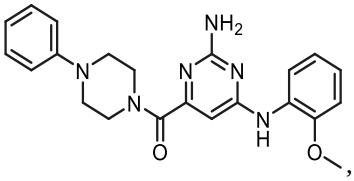
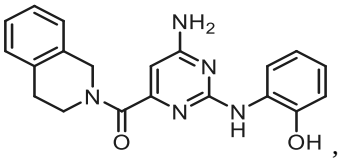
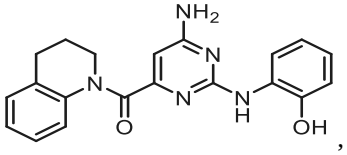
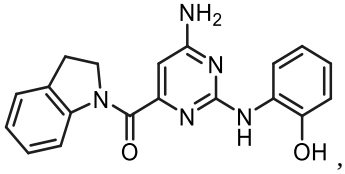
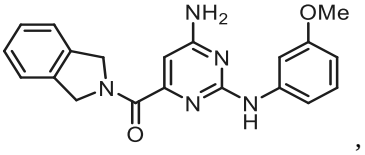
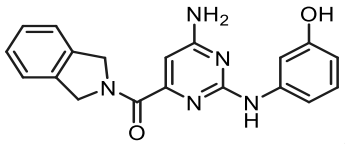
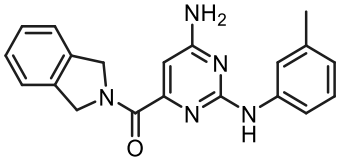
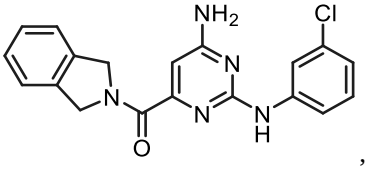
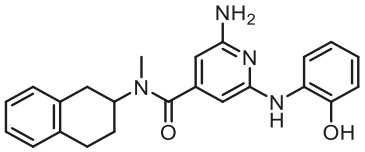
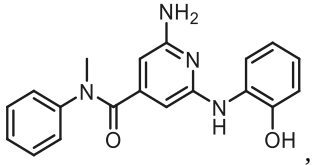
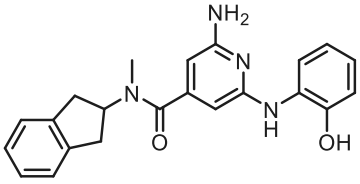
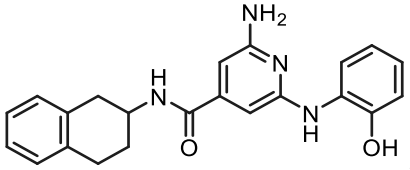
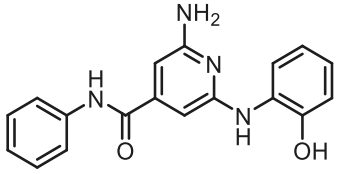
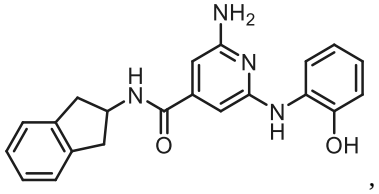
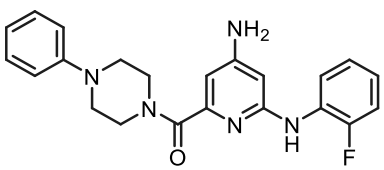
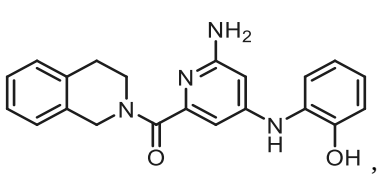
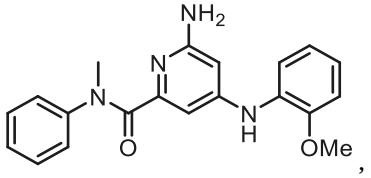
22. The compound of claim 1, which is selected from the group consisting of

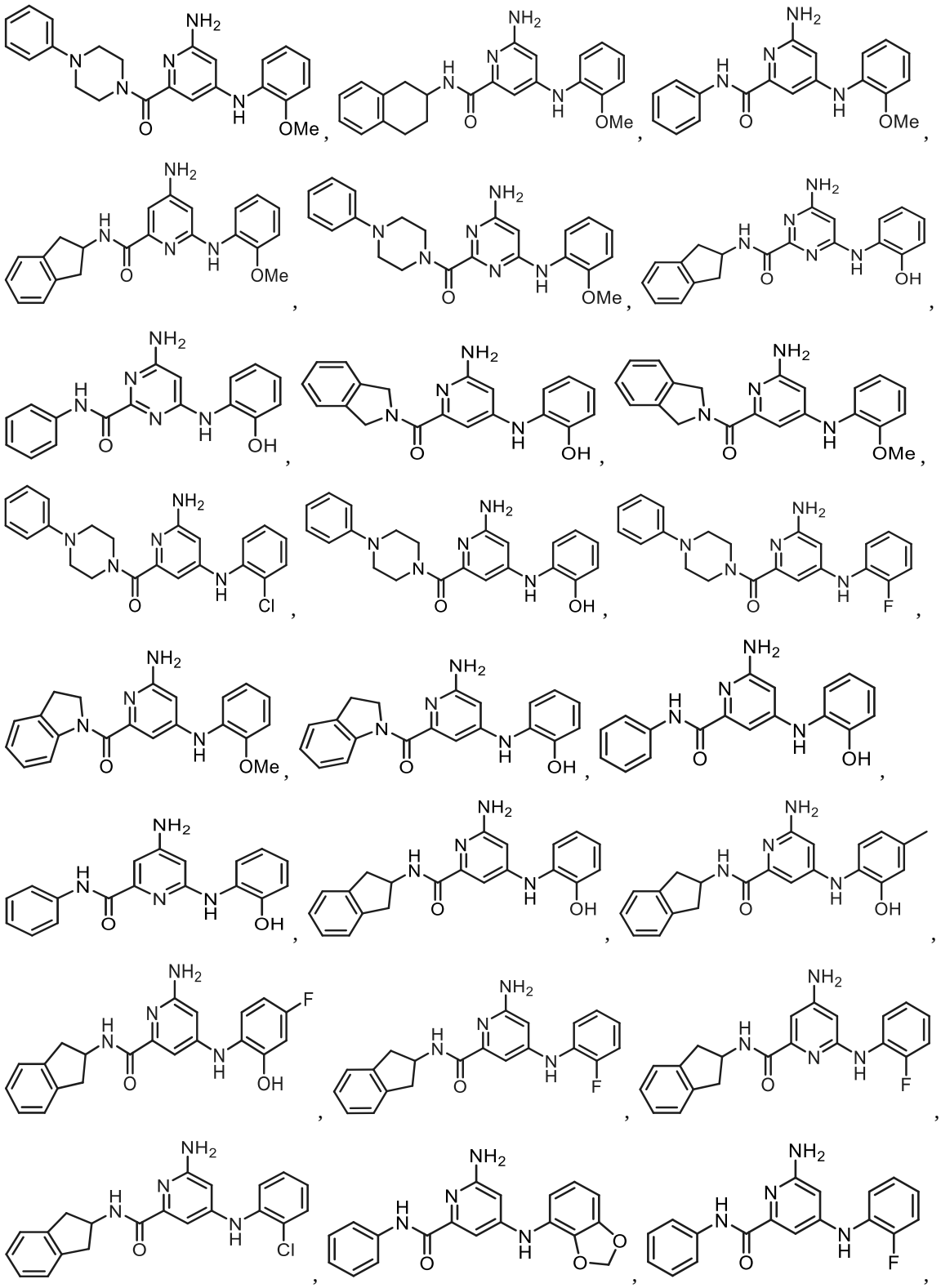
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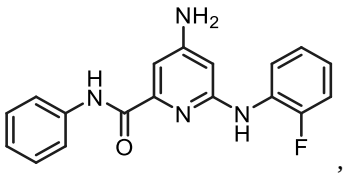
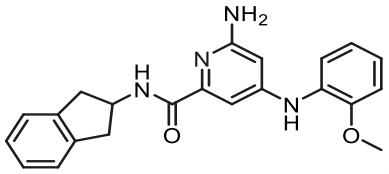
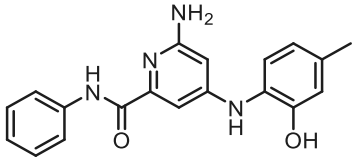
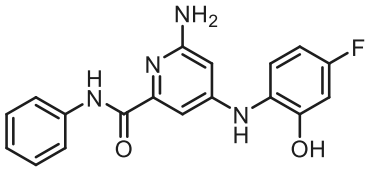
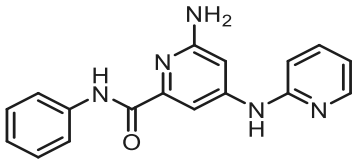
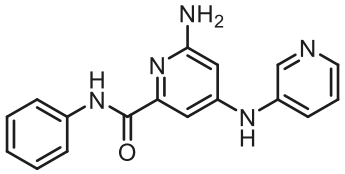
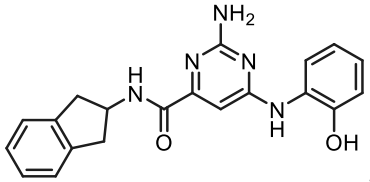
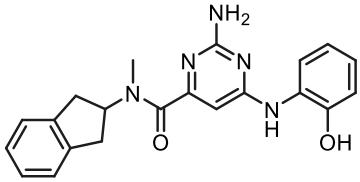
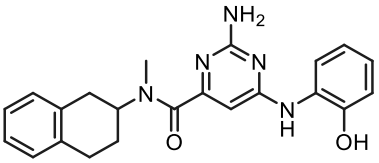
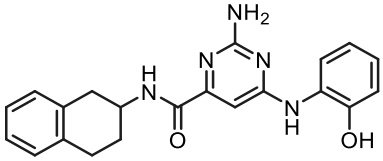
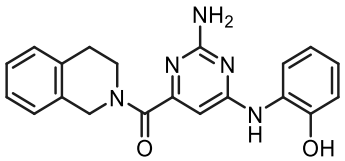
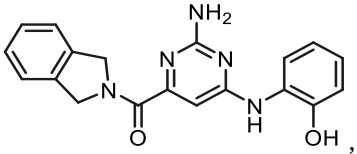
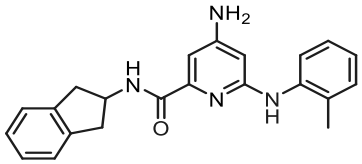
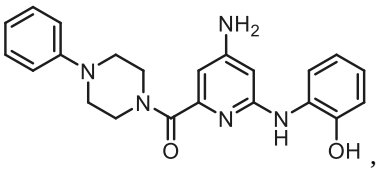
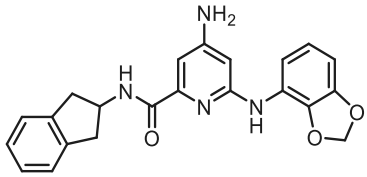
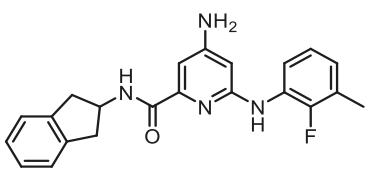
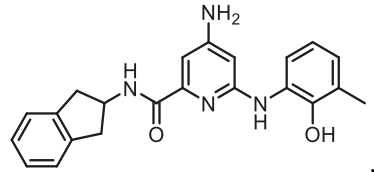
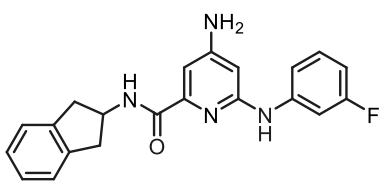
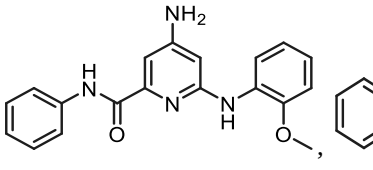
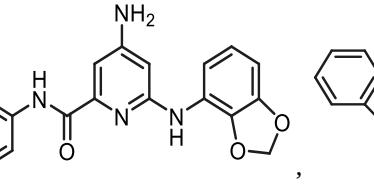
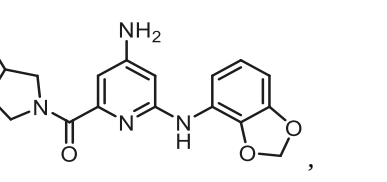
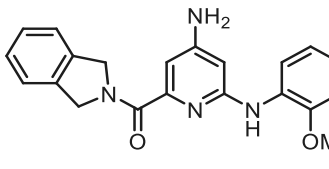
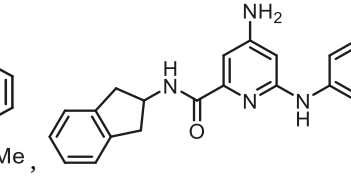
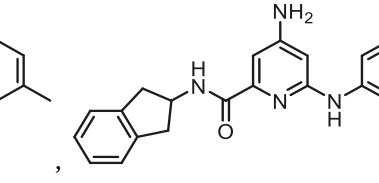
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 , and  , or a pharmaceutically acceptable salt or solvate thereof.

23. The compound of claim 1, which is selected from the group consisting of

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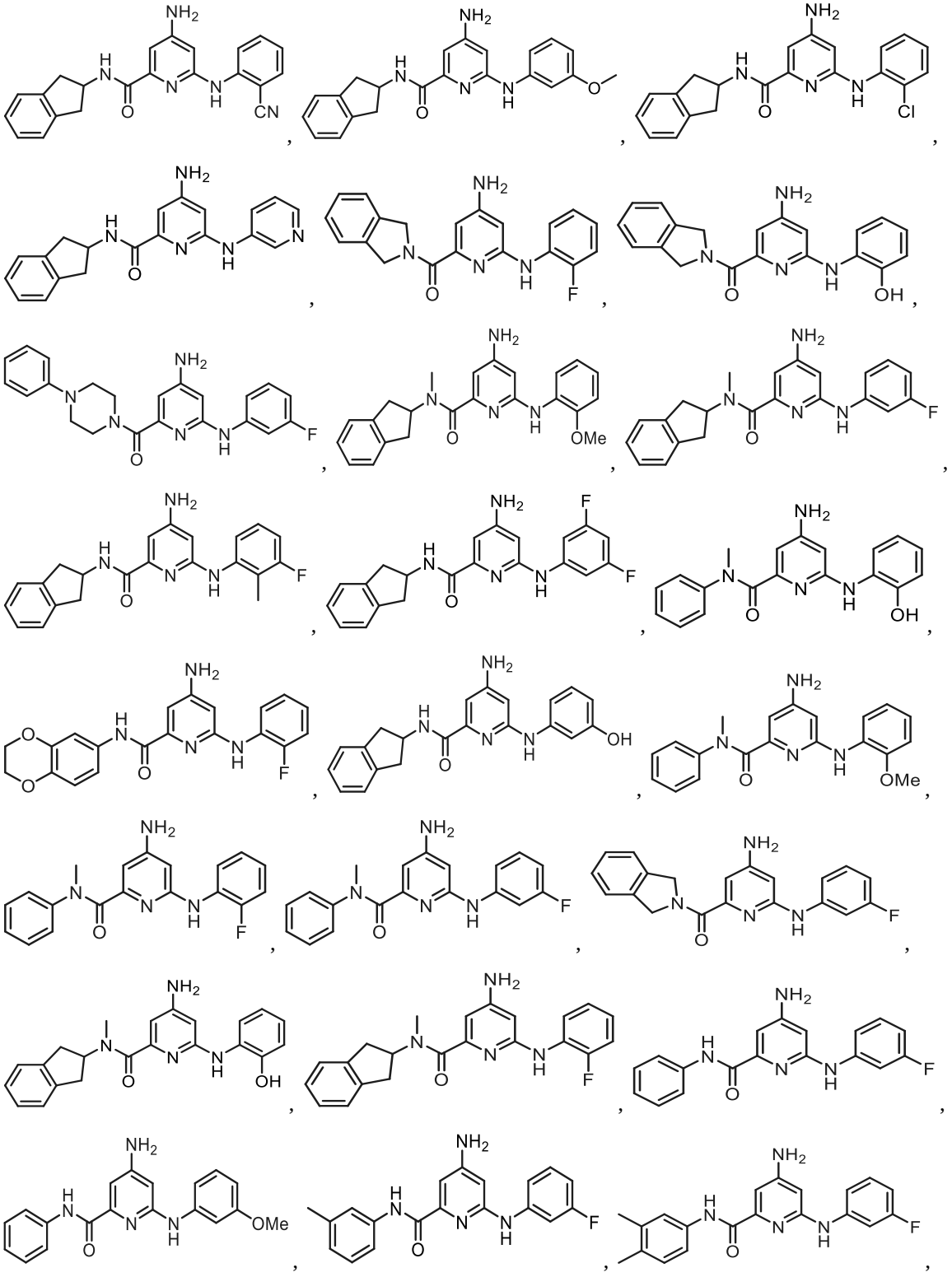


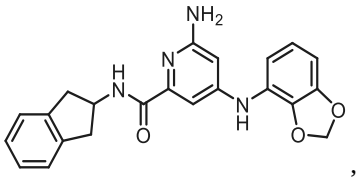
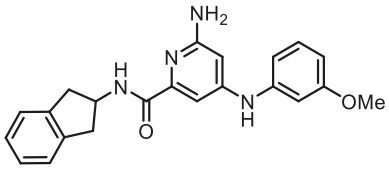
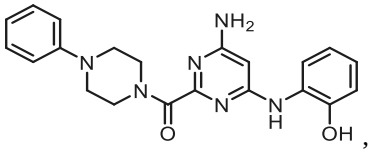
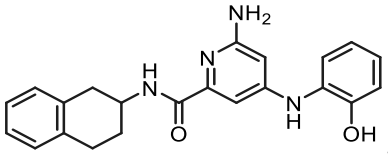
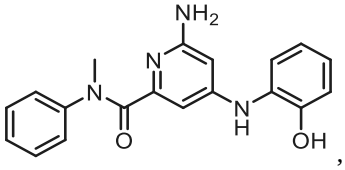
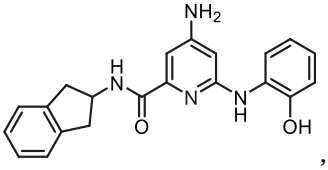
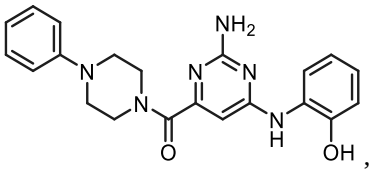
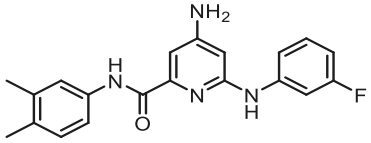

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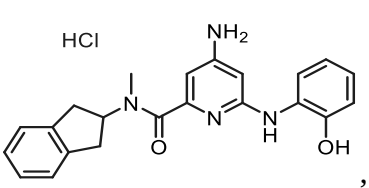
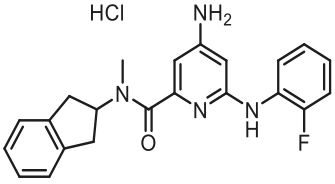
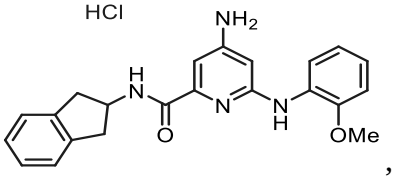
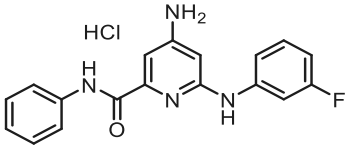
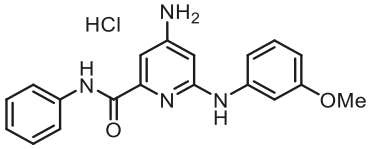
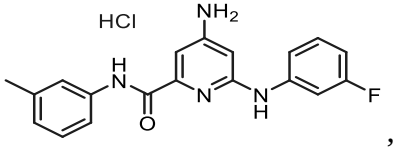
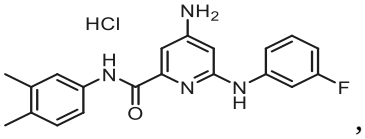
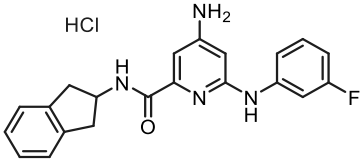
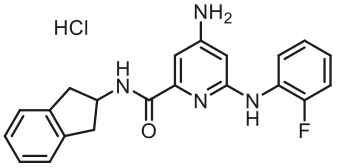
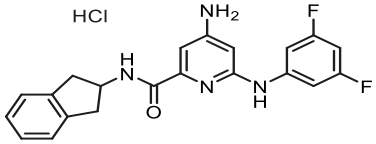
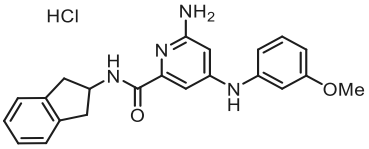
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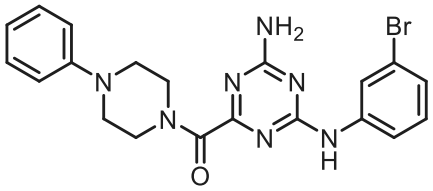
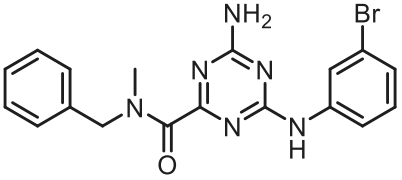
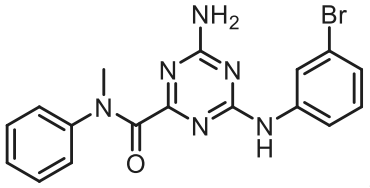
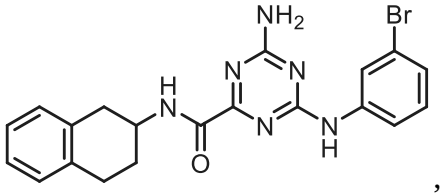
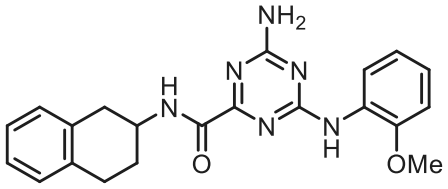
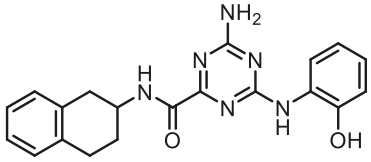

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or a pharmaceutically acceptable acceptable salt or solvate thereof.

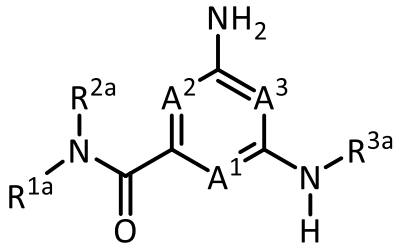
24. The compound of claim 1, selected from the group consisting of


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25. A compound, which is selected from the group consisting of


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or a pharmaceutically aceptable salt or solvate thereof.

26. A pharmaceutical composition, comprising an effective amount of a compound of formula (IA):


(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4}

alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

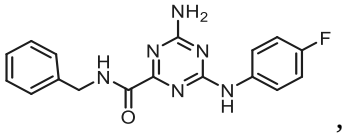
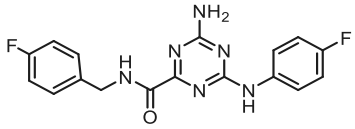
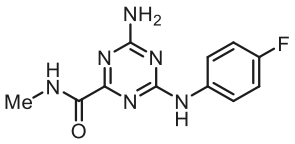
Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

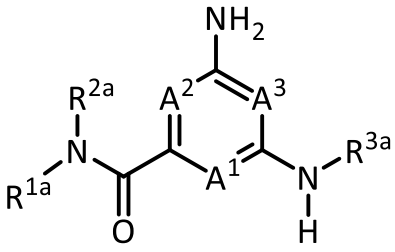
and at least one pharmaceutically acceptable excipient,

with the proviso that the compound is not


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, or 
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27. A pharmaceutical composition, comprising a compound of any one of claims 1-25, or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

28. A compound of formula (IA):


(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and C(R^{4a}), provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

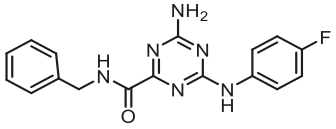
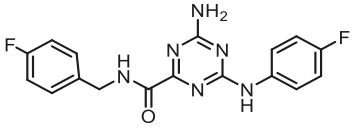
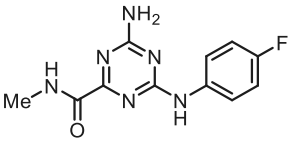
Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

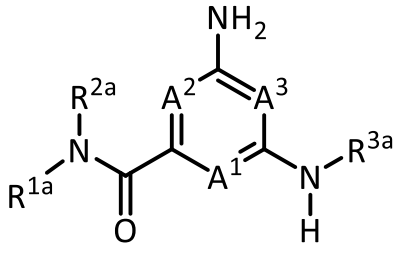
R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

for use as a medicament,

with the proviso that the compound is not


, 
, or 
.

29. A compound of formula (IA):


(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4}

alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

(a) for use in the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient;

(b) for use in the treatment or prevention of a lysosomal storage disease;

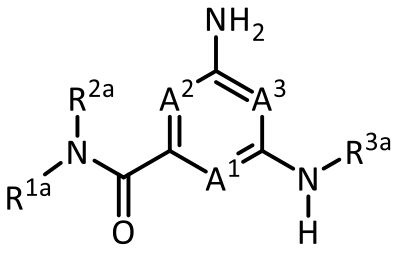
(c) for use in the treatment or prevention of an α-synucleinopathy; or

(d) for use in the treatment or prevention of a disease or disorder, wherein said disease or disorder is selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

30. The compound for use as claimed in claim 29, wherein the lysosomal storage disease is Gaucher’s disease.

31. The compound for use as claimed in any one of claims 28-30, wherein said compound is as claimed in any one of claims 1-25, or a pharmaceutically acceptable salt or solvate thereof.

32. Use of a compound of formula (IA):



(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

A^1, A^2, and A^3 are each independently selected from the group consisting of N, CH and $C(R^{4a})$, provided that at least one of A^1, A^2, or A^3 is N;

each R^{4a} is independently selected from the group consisting of halogen, -C_{1-4} alkyl, -C_{1-4} alkoxy, and -CN;

R^{1a} is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, and –C(=O)Ra^a, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -N$(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and optionally substituted –O-(C_{6-10} aryl); and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring; and

R^{2a} is selected from the group consisting of hydrogen, -C_{1-4} alkyl, and C_{3-6} cycloalkyl, wherein said -C_{1-4} alkyl is optionally substituted; or

R^{1a} and R^{2a} together with the nitrogen atom to which they are attached form an optionally substituted 5- to 10-membered heterocyclic ring, wherein said heterocyclic ring optionally contains 1, 2, or 3 additional heteroatoms selected from the group consisting of N, S, or O, and wherein said heterocyclic ring is optionally fused to a phenyl ring;

Ra^a is selected from the group consisting of -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{6-10} aryl, -C_{1-4} alkyl-C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -(5- to 10-membered)-C_{2-9} heterocyclyl, and -C_{1-4} alkyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl, and -(5- to 10-membered)-C_{2-9} heterocyclyl; and wherein said cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

each Rb^a is independently hydrogen, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, or -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms; and

R^{3a} is selected from the group consisting of -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{3-10} cycloalkyl, and -(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl, and heterocyclyl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^a, -SRb^a, -$N(Rb^a)_2$, -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, -CN, -ORb^a, and -$N(Rb^a)_2$, optionally substituted -C_{6-10} aryl, optionally substituted -(5- to 10-membered)-C_{1-9} heteroaryl and -(5- to 10-membered)-C_{2-9} heterocyclyl, and wherein said -C_{6-10} aryl is optionally fused to a 5- or 6-membered heterocyclic ring,

(a) in the manufacture of a medicament for the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient;

(b) in the manufacture of a medicament for the treatment or prevention of a lysosomal storage disease;

(c) in the manufacture of a medicament for the treatment or prevention of an α-synucleinopathy; or

(d) in the manufacture of a medicament for the treatment or prevention of a disease or disorder selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

33. The use as claimed in claim 32, wherein the lysosomal storage disease is Gaucher’s disease.

34. The use as claimed in claim 32 or claim 33, wherein said compound is as claimed in any one of claims 1-25, or a pharmaceutically acceptable salt of solvate thereof.

35. A pharmaceutical composition as defined in claim 26 or 27 for use as a medicament.

36. A pharmaceutical composition as defined in claim 26 or 27 (a) for use in the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient; (b) for use in the treatment or prevention of a lysosomal storage disease; (c) for use in the treatment or prevention of an α-synucleinopathy; or (d) for use in the treatment or prevention of a disease or disorder, wherein said disease or disorder is selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive

supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

37. The pharmaceutical composition for use of claim 36, wherein said use is for the treatment or prevention of a lysosomal storage disease which is Gaucher’s disease.

38. Use of a pharmaceutical composition as defined in claim 26 or 27 in the manufacture of a medicament (a) for use in the treatment or prevention of a condition associated with the alteration of the activity of β-glucocerebrosidase in a patient; (b) for use in the treatment or prevention of a lysosomal storage disease; (c) for use in the treatment or prevention of an α-synucleinopathy; or (d) for use in the treatment or prevention of a disease or disorder, wherein said disease or disorder is selected from the group consisting of: Gaucher's disease, Parkinson’s disease, dementia with Lewy bodies, diffuse Lewy body disease, multiple system atrophy (MSA), epilepsy, bipolar disorder, schizophrenia, an anxiety disorder, major depression, polycystic kidney disease, type 2 diabetes, open angle glaucoma, multiple sclerosis (MS), multiple myeloma, Alzheimer's disease, amyothophic lateral sclerosis (ALS), corticobasal degeneration, frontotemporal lobe dementia, GBA1 Parkinson, neuronopathic Gaucher's disease, neuroaxonal dystrophy, neurodegenerative diseases with parkinsonism, progressive supranuclear palsy, pure autonomic failure, sporadic Creuzfeldt-Jakob disease, and unimpaired aging.

39. The use of claim 38, wherein said use is for the treatment or prevention of a lysosomal storage disease which is Gaucher’s disease.