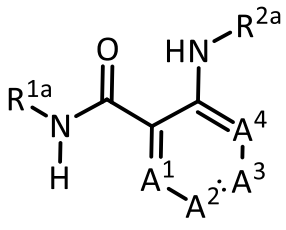
lysosome results in the reduction of lysosome size and correction of the storage. These chaperones may also increase the stability of mutant enzymes toward degradation in the lysosome. *See, e.g.,* Patniak *et al., Journal of Medicinal Chemistry* 55(12):5734-5748 (2012).

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

BRIEF SUMMARY OF THE DISCLOSURE

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

In a first aspect, the present disclosure refers to a use of a compound of formula (IA), or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating or preventing (a) a condition associated with the alteration of the activity of galactocerebrosidase, (b) a lysosomal storage disease or an α-synucleinopathy, or (c) a disease or disorder selected from the group consisting of Krabbe's disease, demyelinating disorders, galactosylsphingosine related disorders, globoid cell leukodystrophy, multiple sclerosis (MS), Parkinson's disease, peripheral neuropathy, progressive multiple sclerosis, pulmonary artery enlargement in COPD, open angle glaucoma, Lewy body dementia, and multiple system atrophy (MSA), in a patient, wherein the compound of formula (IA) has the structure:



(IA),

wherein

A^1, A^2, A^3, and A^4 are each independently selected from the group consisting of N, CH and C(R^{3a});

each R^{3a} is independently selected from the group consisting of halogen, -OH, -C_{1-4} alkyl, halo(C_{1-4} alkyl), -C_{1-4} alkoxy, halo(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, 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; and

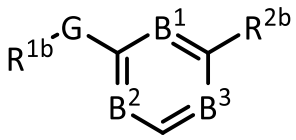
R^{2a} is selected from the group consisting of -C_{1-4} alkyl, -C(=O)Ra^a, -C(=O)NHRa^a, -$S(=O)_2Ra^a$, -C_{1-4} alkyl-C(=O)Ra^a, -C_{1-4} alkyl-C(=O)NHRa^a, -C_{1-4} alkyl-C(=O)$N(Ra^a)_2$, -C_{1-4} alkyl-$S(=O)_2Ra^a$, -C_{1-4} alkyl-$S(=O)_2$-$N(Ra^a)_2$, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -C_{1-4} 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, –C(=O)Ra^a, -ORb^a, -SRb^a, -$N(Rb^a)_2$, (=O), -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;

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; and

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.

In another aspect, the present disclosure refers to a use of a compound of formula (IB), or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating or preventing (a) a condition associated with the alteration of the activity of galactocerebrosidase; (b) a lysosomal storage disease or an α-synucleinopathy, or (c) a disease or disorder selected from the group consisting of Krabbe's disease, demyelinating disorders, galactosylsphingosine related disorders, globoid cell leukodystrophy, multiple sclerosis (MS), Parkinson's disease, peripheral neuropathy, progressive multiple sclerosis, pulmonary artery enlargement in COPD, open angle glaucoma, Lewy body dementia, and multiple system atrophy (MSA), in a patient, wherein the compound of formula (IB) has the structure:



(IB),

wherein

G is -C(=O)-NH- or -NH-C(=O)-;

B^1, B^2, and B^3 are each independently selected from the group consisting of N, CH and C(R^{3b});

each R^{3b} is independently selected from the group consisting of halogen, C$_{1-4}$ alkyl, halo(C$_{1-4}$ alkyl), -OH, C$_{1-4}$ alkoxy, halo(C$_{1-4}$ alkoxy), and CN;

R^{1b} 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, -C$_{2-4}$ alkylene-C$_{6-10}$ aryl, (5- to 10-membered)-C$_{1-9}$ heteroaryl, -C$_{1-4}$ alkyl-(5- to 10-membered)-C$_{1-9}$ heteroaryl, -C$_{2-4}$ alkylene-(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_{2-4} alkenyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, alkenylheteroaryl, 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^b, -SRb^b, -$N(Rb^b)_2$, -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, alkenylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

R^{2b} is -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -C(=O)-NH-Ra^b, -$S(=O)_2$-NH-Ra^b, -C_{1-4} alkyl-$C(=O)Ra^b$, -C_{1-4} alkyl-$S(=O)_2Ra^b$, or | -$N(Rb^b)_2$, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, (=O), -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, CN, -ORb^b, and -$N(Rb^b)_2$, 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 -C_{3-10} cycloalkyl; and wherein said aryl, heteroaryl, and heterocyclyl are optionally fused to a further (second) ring; or

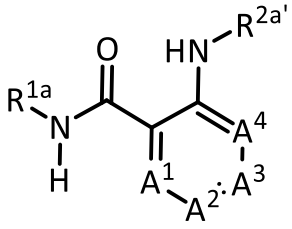
R^{2b} and R^{3b} attached to an adjacent carbon atom together form a 5- or 6-membered heterocyclic ring containing one N-atom substituted with -$S(=O)_2Ra^b$;

Ra^b 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^b, -SRb^b, -$N(Rb^b)_2$, -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; and

each Rb^b is independently hydrogen, $-C(=O)Ra^b$, $-S(=O)_2Ra^b$, $-C_{1-4}$ alkyl, $-C_{3-10}$ cycloalkyl, -(5- to 10-membered)-C_{2-9} heterocyclyl, or optionally substituted $-C_{6-10}$ aryl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms.

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



(IIA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, C_{1-4} alkyl, halo(C_{1-4} alkyl), C_{1-4} alkoxy, halo(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, 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, hydrox, -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;

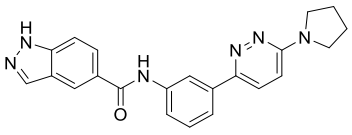
$R^{2a'}$ is selected from the group consisting of $-C(=O)Ra^{a'}$, $-S(=O)_2Ra^{a'}$, $-C_{1-4}$ alkyl-$C(=O)NHRa^{a'}$, $-C_{1-4}$ alkyl-$C(=O)N(Ra^{a'})_2$, $-C_{1-4}$ alkyl-$S(=O)_2$-$N(Ra^{a'})_2$, wherein said alkyl group is optionally substituted with 1, 2 or 3 substituents each independently selected from

the group consisting of halogen, hydroxy, -CN, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms;

$Ra^{a'}$ is selected from the group consisting of -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 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; and

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.

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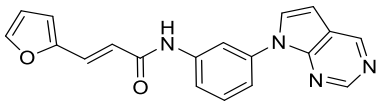
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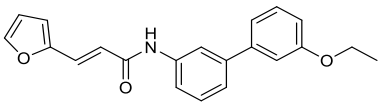
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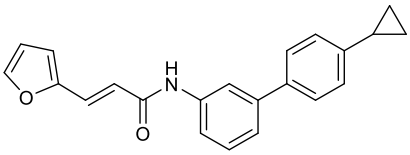
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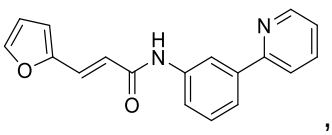
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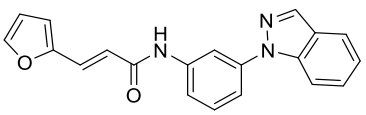
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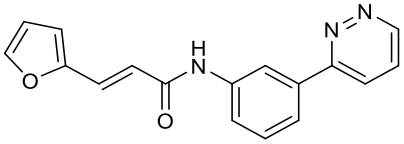
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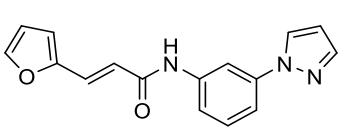
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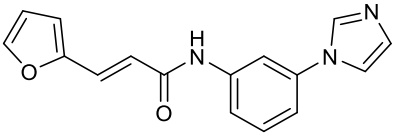
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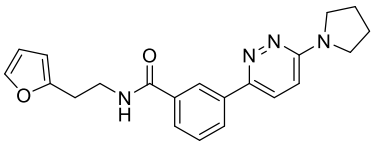
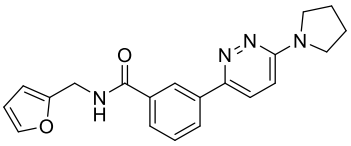
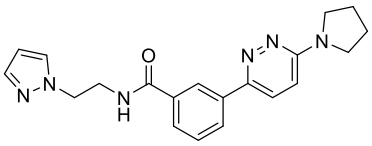
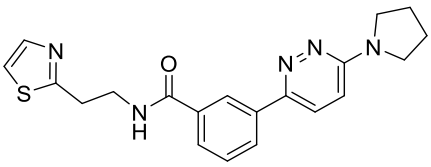
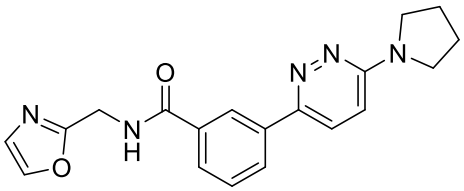
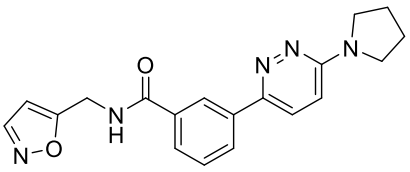
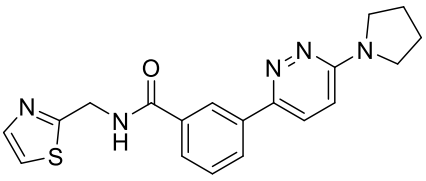
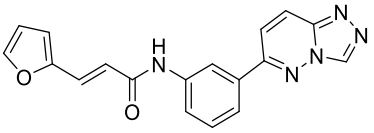
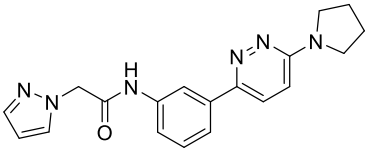
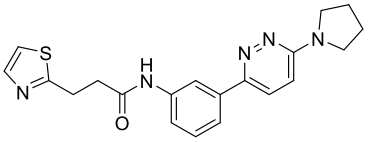
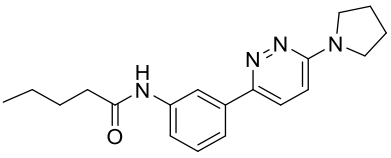
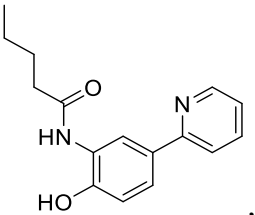
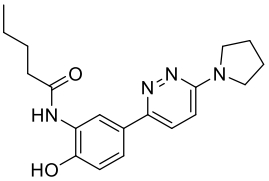
 ,  ,  ,

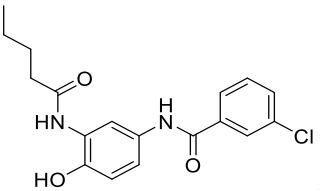
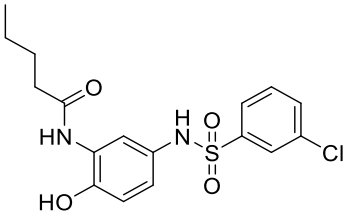
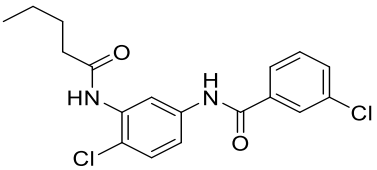
 ,  ,

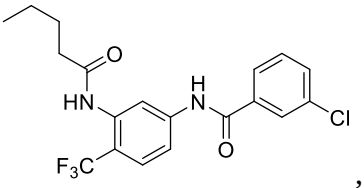
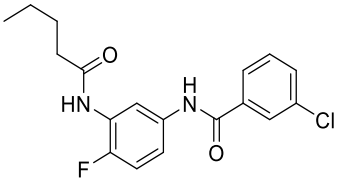
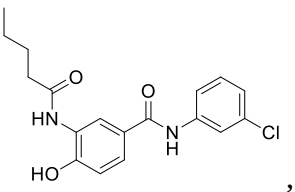
 , and  , or a pharmaceutically acceptable salt or solvate thereof.

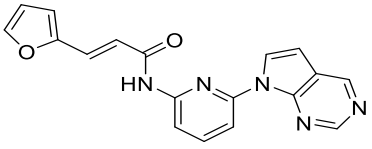
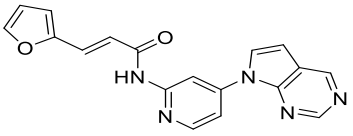
In another aspect, the present disclosure refers to a compound selected from the group consisting of

 ,  ,  ,

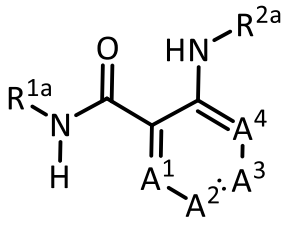
 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 , and  , or a pharmaceutically acceptable 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), or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient, wherein the compound of formula (IA) has the structure:

 (IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, $-C_{1-4}$ alkyl, halo(C_{1-4} alkyl), $-C_{1-4}$ alkoxy, halo(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, 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; and

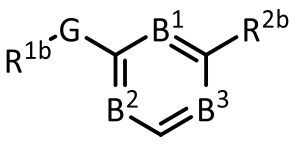
R^{2a} is selected from the group consisting of $-C_{1-4}$ alkyl, $-C(=O)Ra^a$, $-C(=O)NHRa^a$, $-S(=O)_2Ra^a$, $-C_{1-4}$ alkyl-$C(=O)Ra^a$, $-C_{1-4}$ alkyl-$C(=O)NHRa^a$, $-C_{1-4}$ alkyl-$C(=O)N(Ra^a)_2$, $-C_{1-4}$ alkyl-$S(=O)_2Ra^a$, $-C_{1-4}$ alkyl-$S(=O)_2$-$N(Ra^a)_2$, $-C_{1-4}$ alkyl-C_{3-10} cycloalkyl, $-C_{1-4}$ 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, –C(=O)Ra^a, -ORb^a, -SRb^a, -N(Rb^a)$_2$, (=O), -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;

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; and

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.

In a further aspect, the present disclosure refers to a pharmaceutical composition, comprising an effective amount of a compound of formula (IB), or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient, wherein the compound of formula (IB) has the structure:



(IB),

or a pharmaceutically acceptable salt or solvate thereof, wherein

G is -C(=O)-NH- or -NH-C(=O)-;

B^1, B^2, and B^3 are each independently selected from the group consisting of N, CH and $C(R^{3b})$;

each R^{3b} is independently selected from the group consisting of halogen, C_{1-4} alkyl, halo(C_{1-4} alkyl), -OH, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, and CN;

R^{1b} 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, -C_{2-4} alkylene-C_{6-10} aryl, (5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -C_{2-4} alkylene-(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_{2-4} alkenyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, alkenylheteroaryl, 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^b, -SRb^b, -$N(Rb^b)_2$, -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, alkenylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

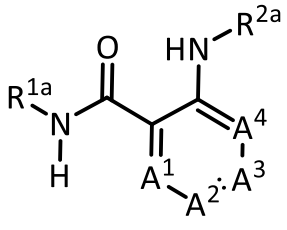
R^{2b} is -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -$C(=O)$-NH-Ra^b, -$S(=O)_2$-NH-Ra^b, -C_{1-4} alkyl-$C(=O)Ra^b$, -C_{1-4} alkyl-$S(=O)_2Ra^b$, or -$N(Rb^b)_2$, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, (=O), -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, CN, -ORb^b, and -$N(Rb^b)_2$, 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 -C_{3-10} cycloalkyl; and wherein said aryl, heteroaryl, and heterocyclyl are optionally fused to a further (second) ring; or

R^{2b} and R^{3b} attached to an adjacent carbon atom together form a 5- or 6-membered heterocyclic ring containing one N-atom substituted with -$S(=O)_2Ra^b$;

Ra^b 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^b, -SRb^b, -$N(Rb^b)_2$, -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; and

each Rb^b is independently hydrogen, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -(5- to 10-membered)-C_{2-9} heterocyclyl, or optionally substituted -C_{6-10} aryl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms.

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



(IA),

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

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, -C_{1-4} alkyl, halo(C_{1-4} alkyl), -C_{1-4} alkoxy, halo(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, 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

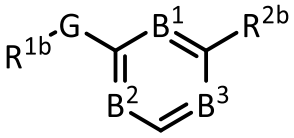
independently selected from the group consisting of halogen, hydroxy, CN, -ORb^a, -SRb^a, -N(Rb^a)$_2$, -C$_{1-4}$ alkyl optionally substituted with 1, 2, or 3 halogen atoms, optionally substituted -C$_{6-10}$ aryl, optionally substituted -(5- to 10-membered)-C$_{1-9}$ heteroaryl, and -(5- to 10-membered)-C$_{2-9}$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

R^{2a} is selected from the group consisting of -C$_{1-4}$ alkyl, -C(=O)Ra^a, -C(=O)NHRa^a, -S(=O)$_2$Ra^a, -C$_{1-4}$ alkyl-C(=O)Ra^a, -C$_{1-4}$ alkyl-C(=O)NHRa^a, -C$_{1-4}$ alkyl-C(=O)N(Ra^a)$_2$, -C$_{1-4}$ alkyl-S(=O)$_2$Ra^a, -C$_{1-4}$ alkyl-S(=O)$_2$-N(Ra^a)$_2$, -C$_{1-4}$ alkyl-C$_{3-10}$ cycloalkyl, -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, –C(=O)Ra^a, -ORb^a, -SRb^a, -N(Rb^a)$_2$, (=O), -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;

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; and

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.

In yet another aspect, the present disclosure refers to a compound of formula (IB) having the structure:



(IB),

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

G is -C(=O)-NH- or -NH-C(=O)-;

B^1, B^2, and B^3 are each independently selected from the group consisting of N, CH and $C(R^{3b})$;

each R^{3b} is independently selected from the group consisting of halogen, C_{1-4} alkyl, halo(C_{1-4} alkyl), -OH, C_{1-4} alkoxy, halo(C_{1-4} alkoxy), and CN;

R^{1b} 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, -C_{2-4} alkylene-C_{6-10} aryl, (5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -C_{2-4} alkylene-(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_{2-4} alkenyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, alkenylheteroaryl, 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^b, -SRb^b, -$N(Rb^b)_2$, -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, alkenylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

R^{2b} is -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -C(=O)-NH-Ra^b, -$S(=O)_2$-NH-Ra^b, -C_{1-4} alkyl-$C(=O)Ra^b$, -C_{1-4} alkyl-$S(=O)_2Ra^b$, or -$N(Rb^b)_2$, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3

substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -N(Rb^b)$_2$, (=O), -C$_{1-4}$alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, CN, -ORb^b, and -N(Rb^b)$_2$, 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 -C$_{3-10}$ cycloalkyl; and wherein said aryl, heteroaryl, and heterocyclyl are optionally fused to a further (second) ring; or

R^{2b} and R^{3b} attached to an adjacent carbon atom together form a 5- or 6-membered heterocyclic ring containing one N-atom substituted with -S(=O)$_2$Ra^b;

Ra^b 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^b, -SRb^b, -N(Rb^b)$_2$, -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; and

each Rb^b is independently hydrogen, -C(=O)Ra^b, -S(=O)$_2$Ra^b, -C$_{1-4}$ alkyl, -C$_{3-10}$ cycloalkyl, -(5- to 10-membered)-C$_{2-9}$ heterocyclyl, or optionally substituted -C$_{6-10}$ aryl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms.

In one example, the present disclosure provides a method of treating or preventing a condition associated with the alteration of the activity of galactocerebrosidase in a patient in need thereof, comprising administering an effective amount of a compound of formula (IA) or formula (IB), or a salt or solvate thereof, as described herein. Compounds represented by formulae (IA) and (IIA), and formulae (IB), (IIB) and (IIIB), and the salts and solvates thereof, are herein collectively referred to as "Compounds of the Disclosure" (each individually referred to as a "Compound of the Disclosure").

In another aspect, the present disclosure provides a method of treating or preventing a lysosomal storage disease, such as Krabbe’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 method of treating or preventing a disease or disorder selected from the group consisting of: Krabbe's disease, demyelinating disorders, galactosylsphingosine related disorders, globoid cell leukodystrophy, multiple sclerosis (MS), Parkinson’s disease, peripheral neuropathy, progressive multiple sclerosis, pulmonary artery enlargement in COPD, open angle

glaucoma, Lewy body dementia, and multiple system atrophy (MSA), comprising administering to a patient in need thereof an effective amount of a Compound of the Disclosure.

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 example, the enzyme is galactocerebrosidase or an analog thereof. 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 therapeutic agent is an effective amount of substrate reduction agent for substrate reduction therapy.

A number of compounds useful in the treatment or prevention of the present disclosure have not been heretofor reported. Thus, one example of the present disclosure is directed to the novel compounds of formulae (IA), (IIA), (IB), (IIB), and (IIIB), and the salts and solvates thereof. Another example of the present disclosure is directed to pharmaceutical compositions comprising these novel compounds of formulae (IA), (IIA), (IB), (IIB), and (IIIB), and the salts and solvates thereof, and at least one pharmaceutically acceptable excipient.

In another example, the present disclosure provides compounds of formula (IA), and the salts and solvates thereof, with the proviso that no more than one of A^1, A^2, A^3, or A^4 is N.

In another example, the present disclosure provides compounds of formula (IIA), and the salts and solvates thereof.

In another example, the present disclosure provides compounds of formula (IIA), and the salts and solvates thereof, with the following provisos: 1) when A^1 is N and $R^{2a'}$ is -C_{1-4} alkyl-C(=O)NHR$a^{a'}$, then R$a^{a'}$ is other than -(5- to 10-membered)-C_{2-9} heterocyclyl; or 2) when A^4 is N, then $R^{2a'}$ is other than -C(=O)R$a^{a'}$.

In another example, the present disclosure provides compounds of formula (IB), and the salts and solvates thereof, with the proviso that no more than one of B^1, B^2, or B^3 is N.

In another example, the present disclosure provides compounds of formulae (IIB) and (IIIB), and the salts and solvates thereof, with the proviso that no more than one of B^1, B^2, or B^3 is N.

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 galactocerebrosidase 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 Krabbe'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: Krabbe's disease, demyelinating disorders, galactosylsphingosine related disorders, globoid cell leukodystrophy, multiple sclerosis (MS), Parkinson's disease, peripheral neuropathy, progressive multiple sclerosis, pulmonary artery enlargement in COPD, open angle glaucoma, Lewy body dementia, and multiple system atrophy (MSA).

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 galactocerebrosidase 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 galactocerebrosidase 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 condition associated with the alteration of the activity of galactocerebrosidase in a patient in need thereof, such as lysosomal storage diseases and α-synucleinopathies described herein.

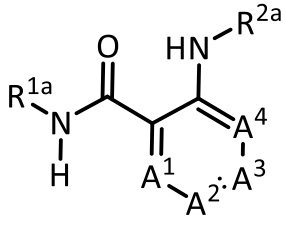
Other examples and advantages of the disclosure will be readily apparent from the following detailed description of the disclosure. The examples and advantages of the disclosure will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

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.

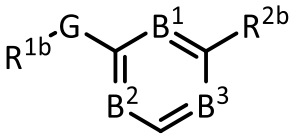
DETAILED DESCRIPTION OF THE DISCLOSURE

One aspect of the disclosure is based on the use of Compounds of the Disclosure for binding to mutated galactocerebrosidase. In view of this property, Compounds of the Disclosure are expected to be useful for treating or preventing, e.g., Krabbe'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):



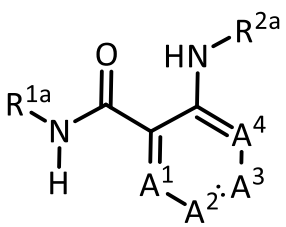
(IA) and



(IB),

and the pharmaceutically acceptable salts and solvates thereof, wherein A^1, A^2, A^3, A^4, R^{1a}, R^{2a}, B^1, B^2, B^3, G, R^{1b}, and R^{2b} are as defined below.

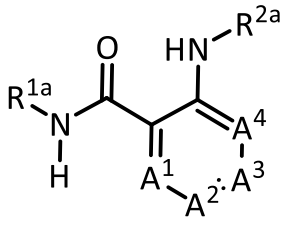
In another aspect, Compounds of the Disclosure are compounds of formula (IA):



(IA),

WHAT IS CLAIMED IS:

1. Use of a compound of formula (IA), or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating or preventing (a) a condition associated with the alteration of the activity of galactocerebrosidase, (b) a lysosomal storage disease or an α-synucleinopathy, or (c) a disease or disorder selected from the group consisting of Krabbe's disease, demyelinating disorders, galactosylsphingosine related disorders, globoid cell leukodystrophy, multiple sclerosis (MS), Parkinson's disease, peripheral neuropathy, progressive multiple sclerosis, pulmonary artery enlargement in COPD, open angle glaucoma, Lewy body dementia, and multiple system atrophy (MSA), in a patient, wherein the compound of formula (IA) has the structure:



(IA),

wherein

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, -C_{1-4} alkyl, halo(C_{1-4} alkyl), -C_{1-4} alkoxy, halo(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, 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; and

R^{2a} is selected from the group consisting of -C_{1-4} alkyl, -C(=O)Ra^a, -C(=O)NHRa^a, -S(=O)$_2Ra^a$, -C_{1-4} alkyl-C(=O)Ra^a, -C_{1-4} alkyl-C(=O)NHRa^a, -C_{1-4} alkyl-C(=O)N(Ra^a)$_2$, -C_{1-4} alkyl-S(=O)$_2Ra^a$, -C_{1-4} alkyl-S(=O)$_2$-N(Ra^a)$_2$, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -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, –C(=O)Ra^a, -ORb^a, -SRb^a, -N(Rb^a)$_2$, (=O), -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;

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; and

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.

2. The use of claim 1, wherein A^1, A^2, A^3, and A^4 are CH;
one of A^1, A^2, A^3, and A^4 is C(R^{3a}) and the ones not C(R^{3a}) are CH;
two of A^1, A^2, A^3, and A^4 is C(R^{3a}) and the ones not C(R^{3a}) are CH;

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

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

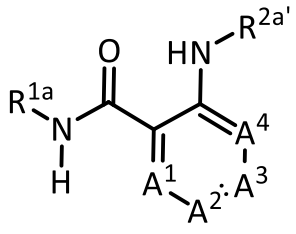
A^3 is N and A^1, A^2, and A^4 are each independently selected from the group consisting of CH and C(R^{3a});

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

two of A^1, A^2, A^3, and A^4 are N, and those that are not N are each independently selected from the group consisting of CH and C(R^{3a}); or

three of A^1, A^2, A^3, and A^4 are N, and the one not N is selected from the group consisting of CH and C(R^{3a}).

3. The use of any one of claims 1-2, wherein the compound of formula (IA) is a compound of formula (IIA):



(IIA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, -C_{1-4} alkyl, halo(C_{1-4} alkyl), -C_{1-4} alkoxy, halo(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, 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, hydrox, -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;

$R^{2a'}$ is selected from the group consisting of -$C(=O)Ra^{a'}$, -$S(=O)_2Ra^{a'}$, -C_{1-4} alkyl-$C(=O)NHRa^{a'}$, -C_{1-4} alkyl-$C(=O)N(Ra^{a'})_2$, -C_{1-4} alkyl-$S(=O)_2$-$N(Ra^{a'})_2$, wherein said alkyl group is optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms;

$Ra^{a'}$ is selected from the group consisting of -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 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; and

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.

4. The use of claim 3, wherein 1) when A^1 is N and $R^{2a'}$ is -C_{1-4} alkyl-$C(=O)NHRa^{a'}$, then $Ra^{a'}$ is other than -(5- to 10-membered)-C_{2-9} heterocyclyl; or 2) when A^4 is N, then $R^{2a'}$ is other than -$C(=O)Ra^{a'}$.

5. The use of any one of claims 1-4, 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 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;

R^{1a} is unsubstituted –C_{1-4} alkyl-C_{6-10} aryl or –C_{1-4} alkyl-C_{6-10} aryl 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;

R^{1a} is unsubstituted benzyl or unsubstituted phenethyl;

R^{1a} is –C_{1-4} alkyl-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 halogen atoms;

R^{1a} is benzyl 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 halogen atoms;

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 above; and wherein said cycloalkyl is optionally fused to a further (second) ring, and wherein Rb^a is as defined in claim 1;

R^{1a} is -(5- to 10-membered)-C_{1-9} heteroaryl or -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, wherein said heteroaryl or alkylheteroaryl 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;

R^{1a} is unsubstituted -(5- to 10-membered)-C_{1-9} heteroaryl or -(5- to 10-membered)-C_{1-9} 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 halogen atoms;

R^{1a} is unsubstituted -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl or -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl 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;

R^{1a} is unsubstituted furan-2-ylmethyl; or

R^{1a} is -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} 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 halogen atoms.

6. The use of any one of claims 1-5, wherein Rb[a] is hydrogen or -C_{1-4} alkyl.

7. The use of any one of claims 1, 2, 5, or 6, wherein R^{2a} is -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, wherein said alkylheteroaryl group is optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, –C(=O)Ra[a], -ORb[a], -SRb[a], -N(Rb[a])$_2$, (=O), -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, wherein Ra[a] and Rb[a] are as claimed in claim 1;

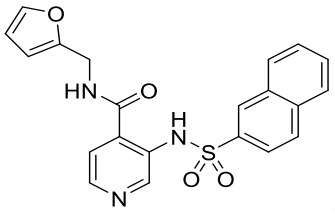
R^{2a} is -C_{1-4} alkyl-C(=O)NHRa[a] or -C_{1-4} alkyl-C(=O)N(Ra[a])$_2$, wherein Ra[a] is as defined in claim 1; or

R^{2a} is –S(=O)$_2$Ra[a], wherein Ra[a] is as defined in claim 1.

8. The use of any one of claims 1, 2, or 5-7, wherein Ra[a] 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 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 aryl, heteroaryl, cycloalkyl, and heterocyclyl is optionally fused to a further (second) ring.

9. The use of claim 3, wherein the compound is selected from the group consisting of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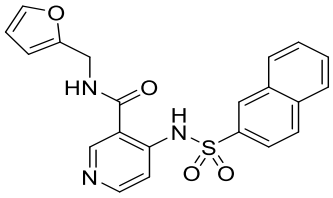
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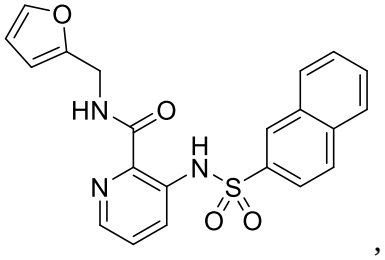
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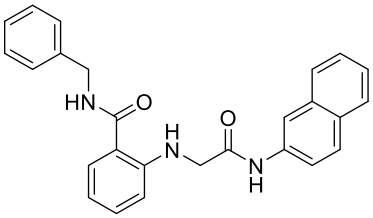
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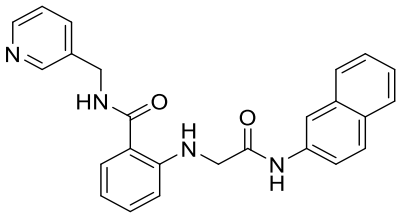
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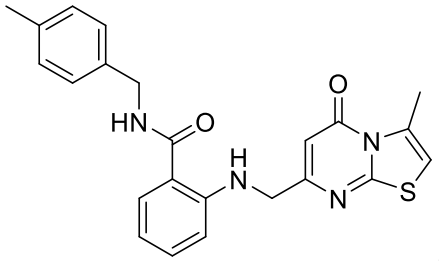
or a pharmaceutically acceptable salt or solvate thereof.

10. The use of any one of claims 1, 2, or 5-8, wherein the compound of formula (IA) is selected from the group consisting of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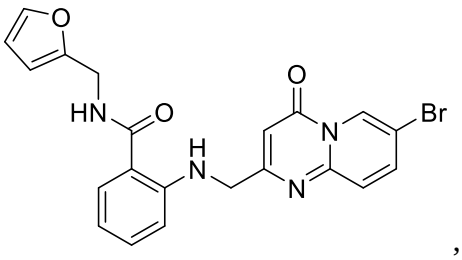
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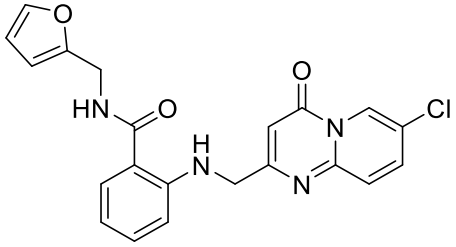
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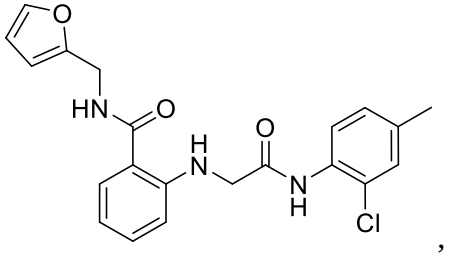
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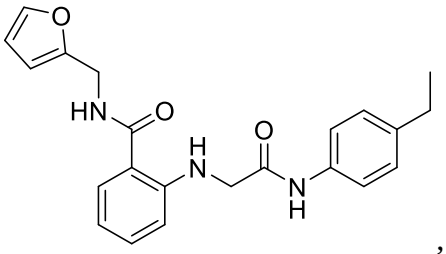
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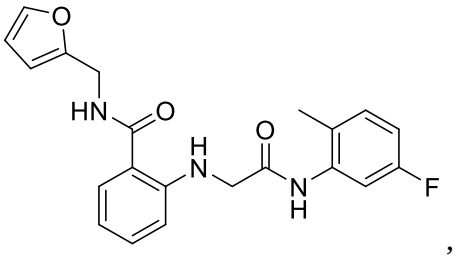
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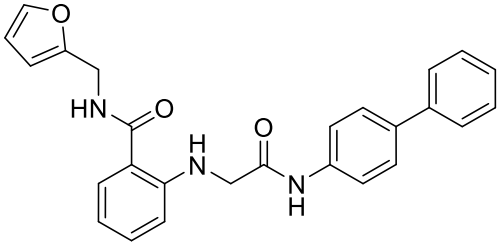
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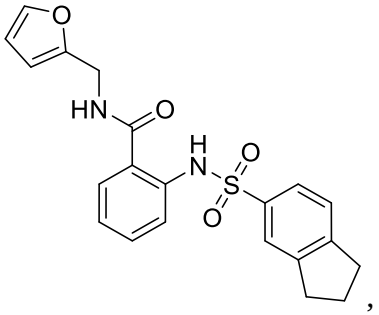
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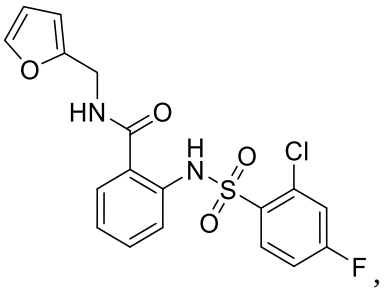
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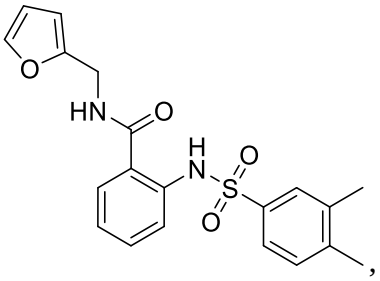
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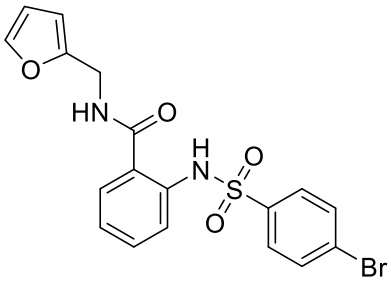
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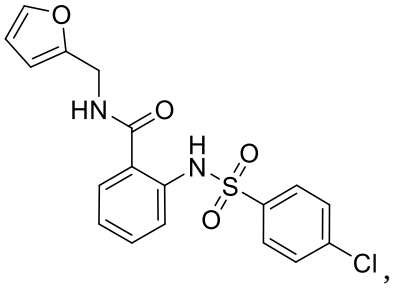
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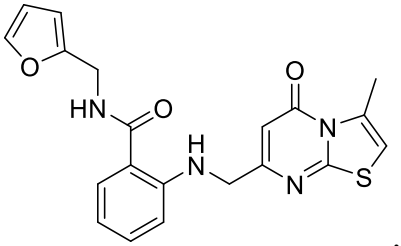
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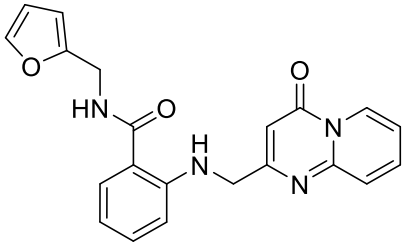
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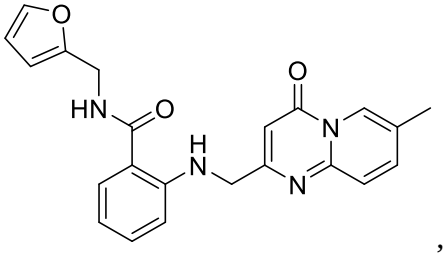
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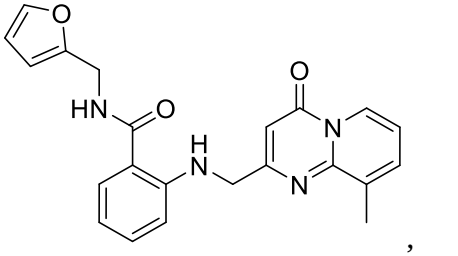
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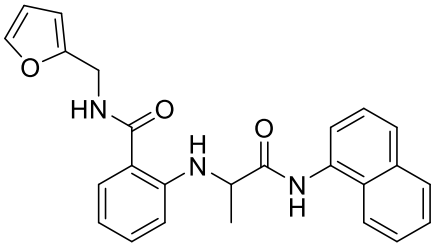
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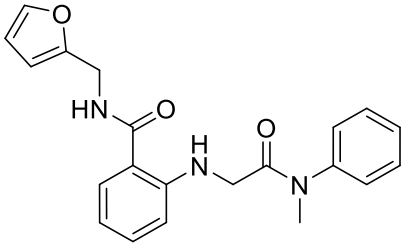
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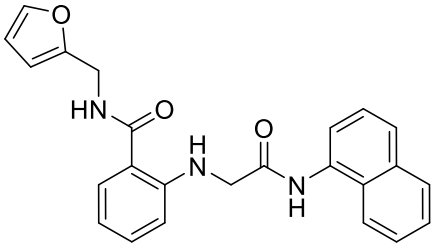
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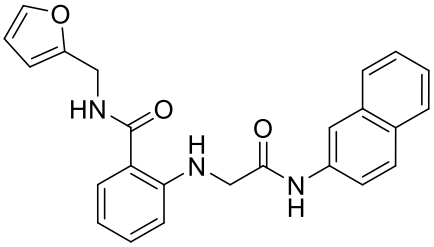
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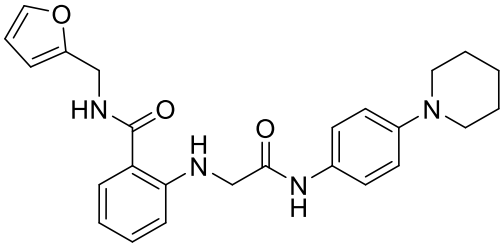
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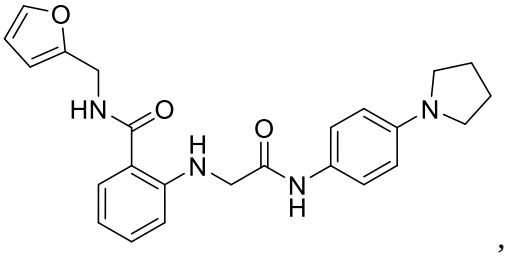
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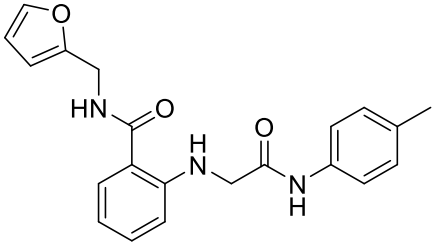
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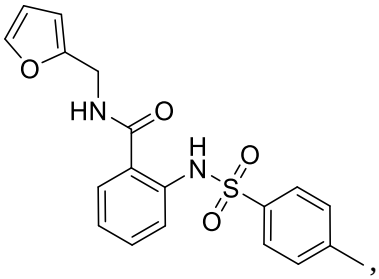
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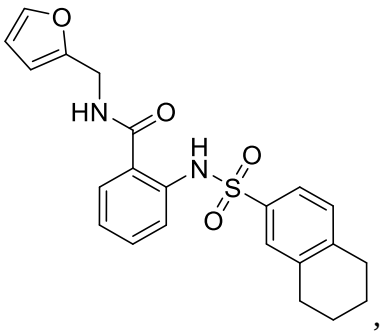
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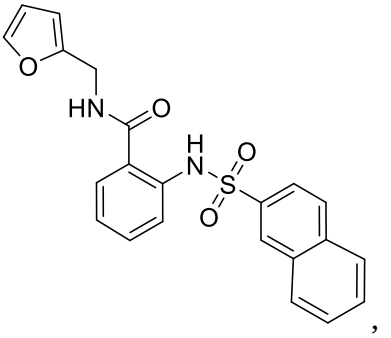
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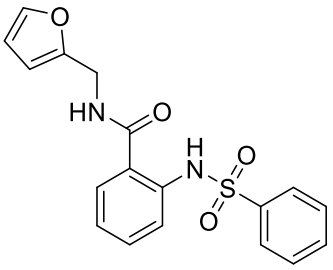
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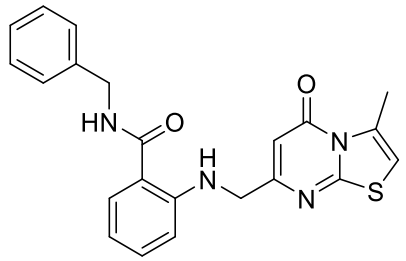
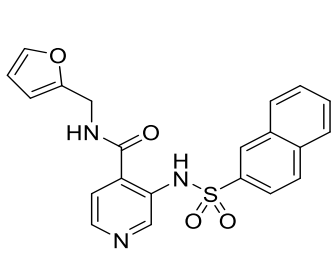
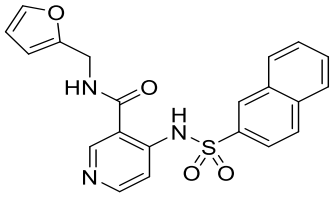
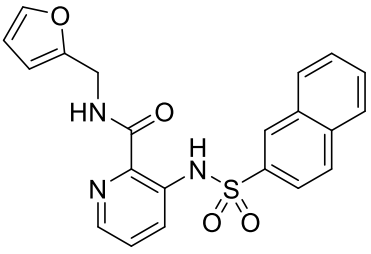
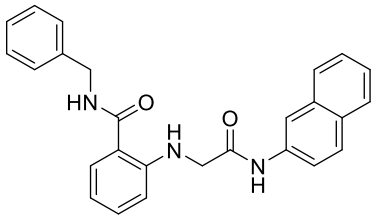
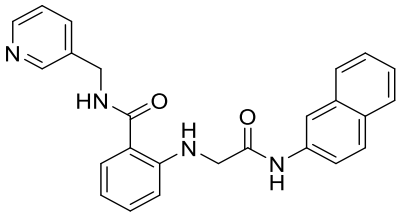
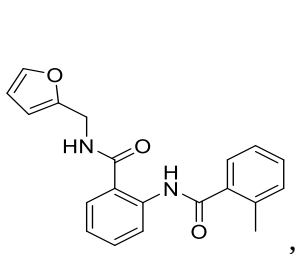
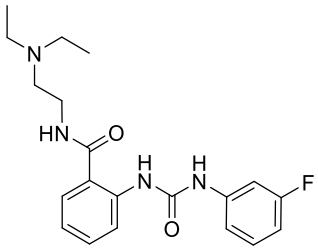
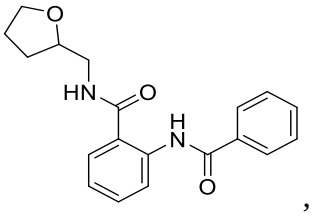
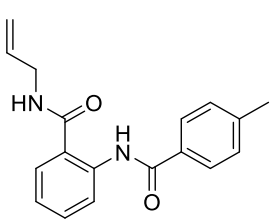
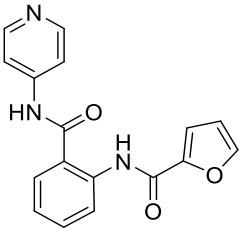
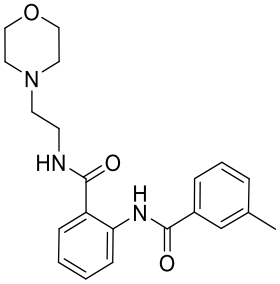
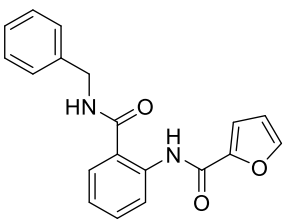
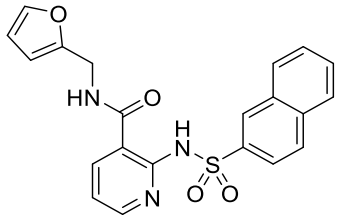
and  , or a pharmaceutically acceptable salt or solvate thereof.

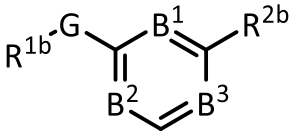
11. The use of any one of claims 1, 2, or 5-8, wherein the compound of formula (IA) is selected from the group consisting of

 ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and



, or a pharmaceutically acceptable salt or solvate thereof.

12. Use of a compound of formula (IB), or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating or preventing (a) a condition associated with the alteration of the activity of galactocerebrosidase; (b) a lysosomal storage disease or an α-synucleinopathy, or (c) a disease or disorder selected from the group consisting of Krabbe's disease, demyelinating disorders, galactosylsphingosine related disorders, globoid cell leukodystrophy, multiple sclerosis (MS), Parkinson's disease, peripheral neuropathy, progressive multiple sclerosis, pulmonary artery enlargement in COPD, open angle glaucoma, Lewy body dementia, and multiple system atrophy (MSA), in a patient, wherein the compound of formula (IB) has the structure:



(IB),

wherein

G is -C(=O)-NH- or -NH-C(=O)-;

B^1, B^2, and B^3 are each independently selected from the group consisting of N, CH and $C(R^{3b})$;

each R^{3b} is independently selected from the group consisting of halogen, C_{1-4} alkyl, halo(C_{1-4} alkyl), -OH, C_{1-4} alkoxy, halo(C_{1-4} alkoxy), and CN;

R^{1b} 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, -C_{2-4} alkylene-C_{6-10} aryl, (5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -C_{2-4} alkylene-(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_{2-4} alkenyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, alkenylheteroaryl, 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^b, -SRb^b, -N(Rb^b)$_2$, -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, alkenylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

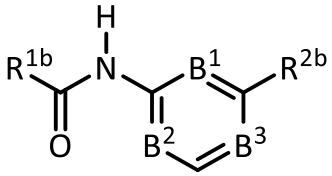
R^{2b} is -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C(=O)Ra^b, -S(=O)$_2Ra^b$, -C(=O)-NH-Ra^b, -S(=O)$_2$-NH-Ra^b, -C_{1-4} alkyl-C(=O)Ra^b, -C_{1-4} alkyl-S(=O)$_2Ra^b$, or | -N(Rb^b)$_2$, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -N(Rb^b)$_2$, (=O), -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, CN, -ORb^b, and -N(Rb^b)$_2$, 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 -C_{3-10} cycloalkyl; and wherein said aryl, heteroaryl, and heterocyclyl are optionally fused to a further (second) ring; or

R^{2b} and R^{3b} attached to an adjacent carbon atom together form a 5- or 6-membered heterocyclic ring containing one N-atom substituted with -S(=O)$_2Ra^b$;

Ra^b 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^b, -SRb^b, -N(Rb^b)$_2$, -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; and

each Rb^b is independently hydrogen, -C(=O)Ra^b, -S(=O)$_2Ra^b$, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -(5- to 10-membered)-C_{2-9} heterocyclyl, or optionally substituted -C_{6-10} aryl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms.

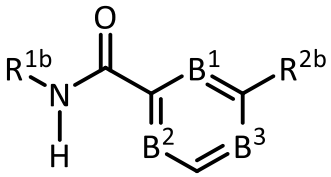
13. The use of claim 12, wherein the compound is a compound of formula (IB) where G is -C(=O)-NH-, having the structure of formula (IIB):



(IIB),

or a pharmaceutically acceptable salt or solvate thereof, wherein B^1, B^2, B^3, R^{1b}, and R^{2b} are as defined in claim 12.

14. The use of claim 12, wherein the compound is a compound of formula (IB) where G is -NH-C(=O)-, having the structure of formula (IIIB):



(IIIB),

or a pharmaceutically acceptable salt or solvate thereof, wherein B^1, B^2, B^3, R^{1b}, and R^{2b} are as defined in claim 12.

15. The use of any one of claims 12-14, wherein B^1, B^2, and B^3 are CH;
one of B^1, B^2, and B^3 is $C(R^{3b})$ and the ones not $C(R^{3b})$ are CH;
two of B^1, B^2, and B^3 is $C(R^{3b})$ and the one not $C(R^{3b})$ is CH;
one of B^1, B^2 and B^3 is N;
two of B^1, B^2 and B^3 are N;
B^1, B^2 and B^3 are N;
B^1 is N and B^2 and B^3 are each independently selected from the group consisting of CH and $C(R^{3b})$;
B^2 is N and B^1 and B^3 are each independently selected from the group consisting of CH and $C(R^{3b})$;
B^3 is N and B^1 and B^2 are each independently selected from the group consisting of CH and $C(R^{3b})$;
B^1 and B^2 are both N and B^3 is CH or $C(R^{3b})$;
B^1 and B^3 are both N and B^2 is CH or $C(R^{3b})$; or
B^2 and B^3 are both N and B^1 is CH or $C(R^{3b})$.

16. The use of any one of claims 12-15, wherein R^{1b} 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 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, -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^b is as defined in claim 12;

R^{1b} is unsubstituted –C_{1-4} alkyl-C_{6-10} aryl or –C_{1-4} alkyl-C_{6-10} aryl optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, -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^b is as defined in claim 12;

R^{1b} is –C_{1-4} alkyl-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 halogen atoms;

R^{1b} 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^b, -SRb^b, -$N(Rb^b)_2$, -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^b is as defined in claim 12; and wherein said cycloalkyl is optionally fused to a further (second) ring;

R^{1b} is -(5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, or –C_{2-4} alkenyl-(5- to 10-membered)-C_{1-9} heteroaryl, wherein said heteroaryl, alkylheteroaryl, or alkenylheteroaryl is optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, -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^b is as defined in claim 12;

R^{1b} is unsubstituted -(5- to 10-membered)-C_{1-9} heteroaryl or -(5- to 10-membered)-C_{1-9} 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 halogen atoms;

R^{1b} is unsubstituted -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl or -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl 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^b is as defined in claim 12;

R^{1b} is unsubstituted –C_{2-4} alkenyl-(5- to 10-membered)-C_{1-9} heteroaryl or –C_{2-4} alkenyl-(5- to 10-membered)-C_{1-9} heteroaryl 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^b is as defined in claim 12;

R^{1b} is unsubstituted furan-2-yl-ethenyl;

R^{1b} is -C_{1-4} alkyl optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^b, -SRb^b, -N(Rb^b)$_2$, -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, alkenylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring, wherein Rb^b is as defined in claim 12;

R^{1b} is unsubstituted -C_{1-4} alkyl; or

R^{1b} is -C_{1-4} alkyl substituted with -ORb^b, -SRb^b, or -N(Rb^b)$_2$, wherein Rb^b is as defined in claim 12.

17. The use of any one of claims 12-16, wherein each Rb^b is independently hydrogen, -C(=O)Ra^b, -S(=O)$_2$Ra^b, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -(5- to 10-membered)-C_{2-9} heterocyclyl, or optionally substituted -C_{6-10} aryl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms.

18. The use of any one of claims 12-17, wherein R^{2b} is -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -C(=O)Ra^b, -S(=O)$_2$Ra^b, -C(=O)-NH-Ra^b, -S(=O)$_2$-NH-Ra^b, -C_{1-4} alkyl-

$C(=O)Ra^b$, -C_{1-4} alkyl-$S(=O)_2Ra^b$, or -$N(Rb^b)_2$, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, (=O), -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, CN, -ORb^b, and -$N(Rb^b)_2$, 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 -C_{3-10} cycloalkyl; and wherein said aryl, heteroaryl, and heterocyclyl is optionally fused to a further (second) ring;

R^{2b} is -C_{6-10} aryl or -(5- to 10-membered)-C_{1-9} heteroaryl, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, (=O), -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, CN, -ORb^b, and -$N(Rb^b)_2$, 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 -C_{3-10} cycloalkyl; and wherein said aryl, heteroaryl, and heterocyclyl is optionally fused to a further (second) ring; wherein Rb^b is as defined in claim 12;

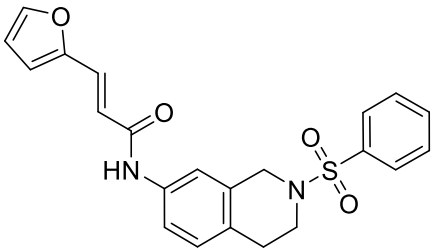
R^{2b} is -$S(=O)_2Ra^b$, -$C(=O)$-NH-Ra^b, -$S(=O)_2$-NH-Ra^b, -C_{1-4} alkyl-$C(=O)Ra^b$, -C_{1-4} alkyl-$S(=O)_2Ra^b$, or -$N(Rb^b)_2$, wherein wherein Ra^b and Rb^b are as defined in claim 12; or

R^{2b} is -$C(=O)$-NH-Ra^b or -$S(=O)_2$-NH-Ra^b, wherein Ra^b is -C_{6-10} aryl optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, and -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms.

19. The use of any one of claims 12-17, wherein R^{2b} and R^{3b} attached to an adjacent carbon atom together form a 5- or 6-membered N-containing heterocyclic ring substituted at the N-atom with -$S(=O)_2Ra^b$; wherein Ra^b is as defined in claim 12.

20. The use of any one of claims 12-19, wherein Rb^b is hydrogen, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -C_{1-4} alkyl, -C_{3-6} cycloalkyl, -(5- to 6-membered)-C_{2-9} heterocyclyl, or -C_{6-10} aryl optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -O(C_{1-4} alkyl) , -S(C_{1-4} alkyl), -NH(C_{1-4} alkyl), -N(C_{1-4} alkyl)$_2$, and -C_{1-4}alkyl optionally substituted by 1, 2 or 3 fluorine atoms.

21. The use of any one of claims 12-14, wherein the compound is selected from the group consisting of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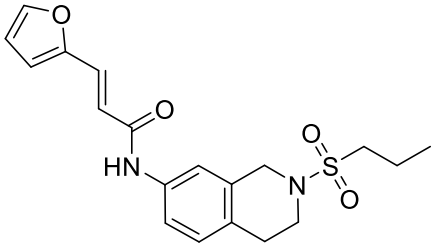
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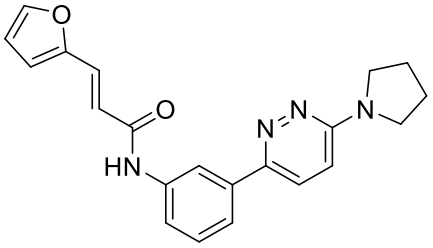
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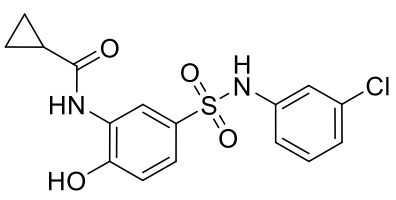
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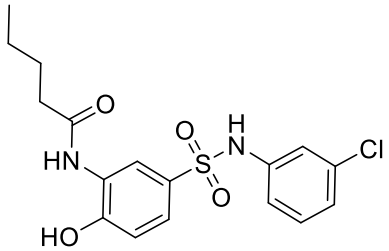
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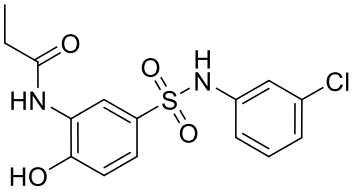
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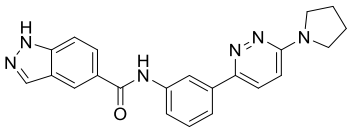
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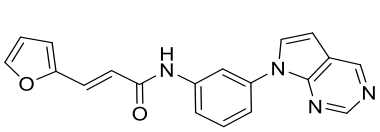
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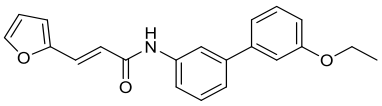
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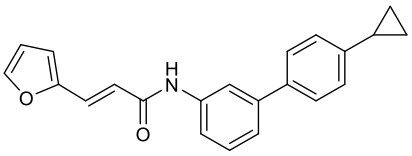
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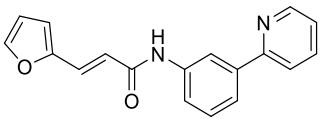
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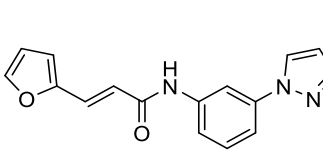
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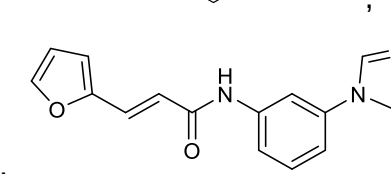
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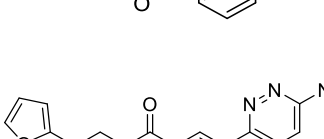
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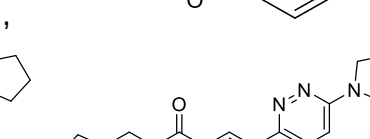
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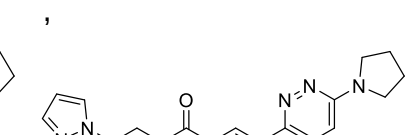
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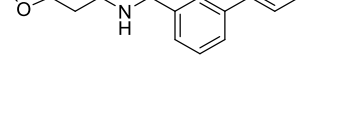
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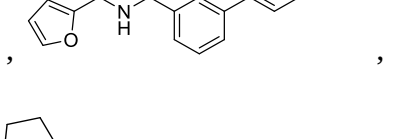
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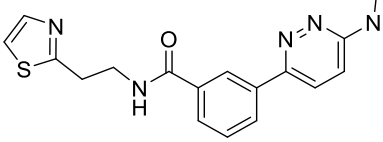
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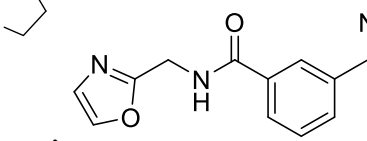
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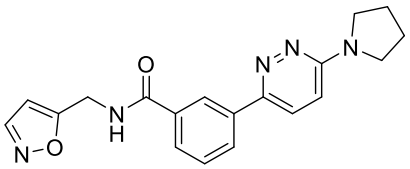
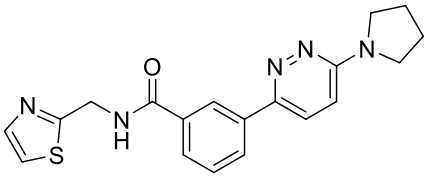
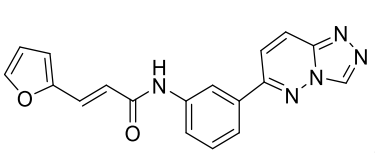
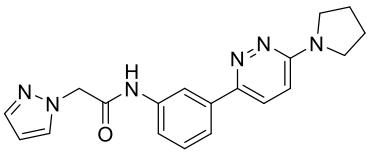
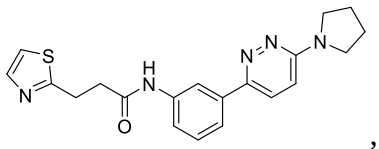
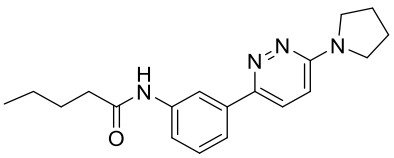
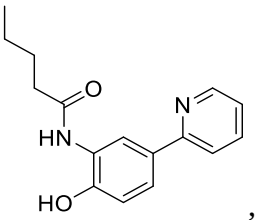
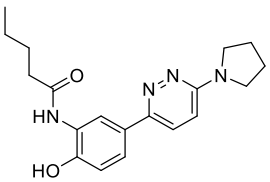
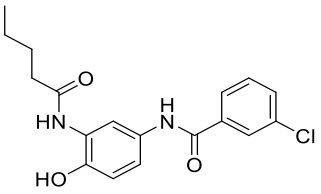
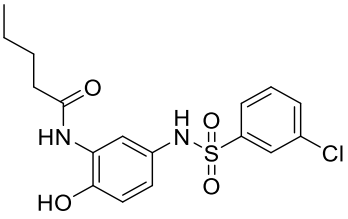
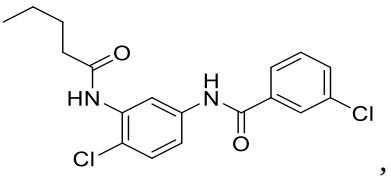
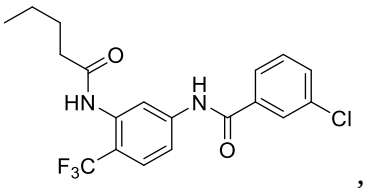
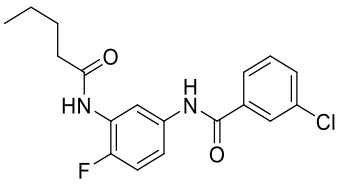
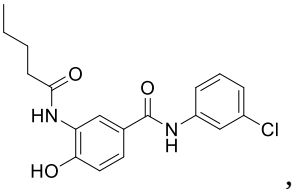
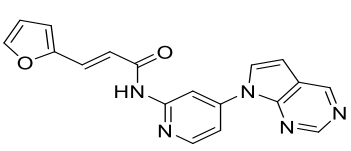
 , and  , or a pharmaceutically acceptable salt or solvate thereof.

22. The use of claim 12 or claim 13, wherein the compound is selected from the group consisting of

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

23. The use of any one of claims 1-22, wherein the medicament is for the treatment or prevention of a lysosomal storage disease.

24. The use of claim 23, wherein the lysosomal storage disease is Krabbe's disease.

25. The use of any one of claims 1-22, wherein the medicament is for the treatment or prevention of an α-synucleinopathy.

26. The use of any one of claims 1-25, wherein the medicament is to be administered together with at least one other therapeutic agent.

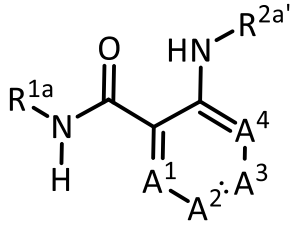
27. The use of claim 26, wherein the therapeutic agent is an effective amount of an enzyme for enzyme replacement therapy or a small molecule chaperone.

28. The use of claim 27, wherein the enzyme is galactocerebrosidase or an analog thereof.

29. The use of claim 27, wherein the small molecule chaperone binds competitively to an enzyme.

30. The use of claims 27 or 29, wherein the small molecule chaperone is selected from the group consisting of iminoalditols, iminosugars, aminosugars, thiophenylglycosides, glycosidase, sulfatase, glycosyl transferase, phosphatase, and peptidase inhibitors.

31. A compound of formula (IIA):



(IIA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, C_{1-4} alkyl, halo(C_{1-4} alkyl), C_{1-4} alkoxy, halo(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, 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, hydrox, -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;

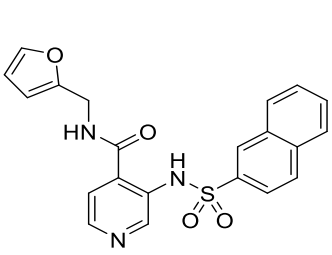
$R^{2a'}$ is selected from the group consisting of -$C(=O)Ra^{a'}$, -$S(=O)_2Ra^{a'}$, -C_{1-4} alkyl-$C(=O)NHRa^{a'}$, -C_{1-4} alkyl-$C(=O)N(Ra^{a'})_2$, -C_{1-4} alkyl-$S(=O)_2$-$N(Ra^{a'})_2$, wherein said alkyl group is optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms;

$Ra^{a'}$ is selected from the group consisting of -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 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; and

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.

32. The compound of claim 31, wherein 1) when A^1 is N and $R^{2a'}$ is -C_{1-4} alkyl-$C(=O)NHRa^{a'}$, then $Ra^{a'}$ is other than -(5- to 10-membered)-C_{2-9} heterocyclyl; or 2) when A^4 is N, then $R^{2a'}$ is other than -$C(=O)Ra^{a'}$.

33. The compound of claim 31, wherein the compound is selected from the group consisting of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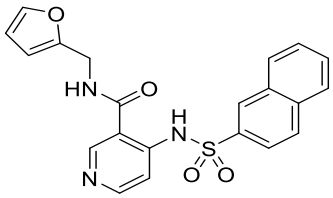
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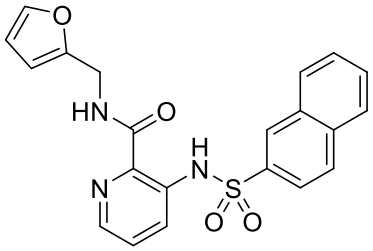
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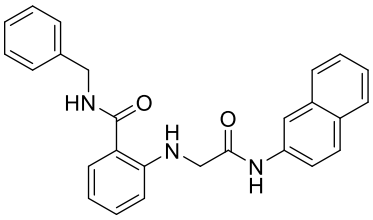
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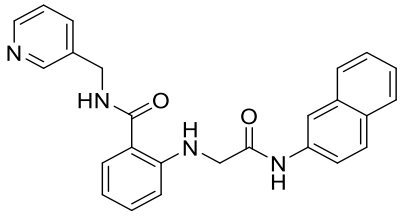
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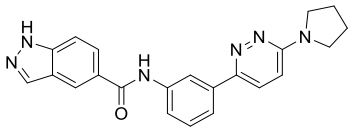
or a pharmaceutically acceptable salt or solvate thereof.

34. A compound selected from the group consisting of compound is selected from the group consisting of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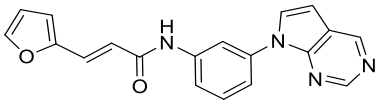
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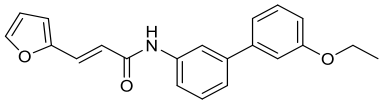
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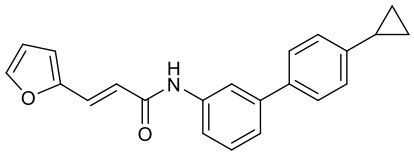
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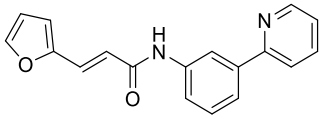
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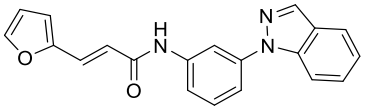
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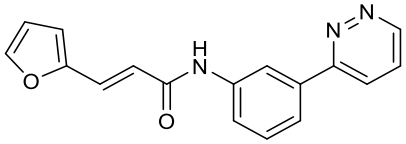
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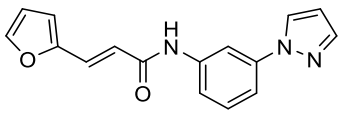
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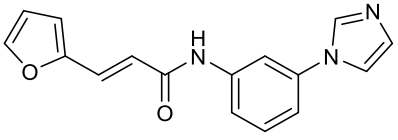
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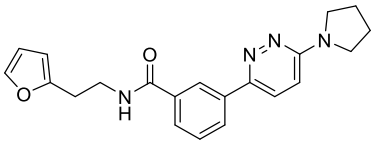
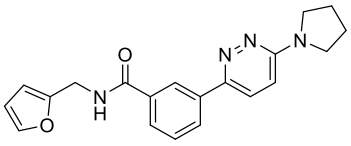
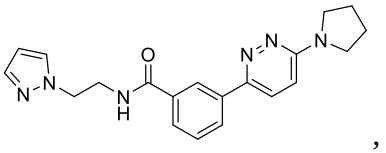
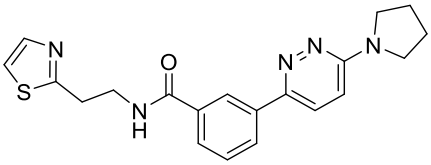
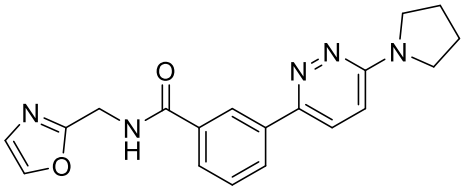
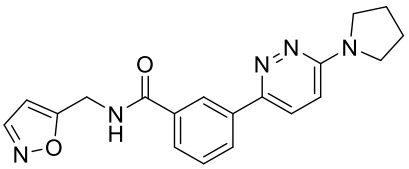
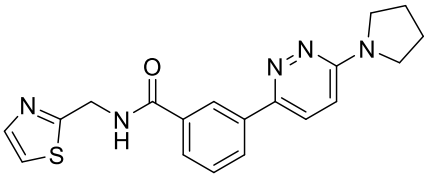
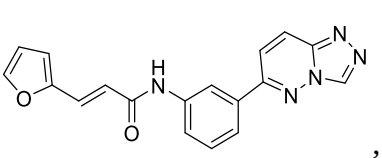
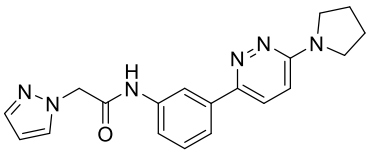
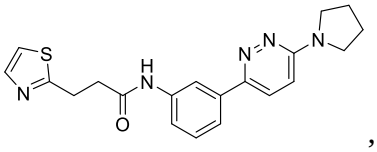
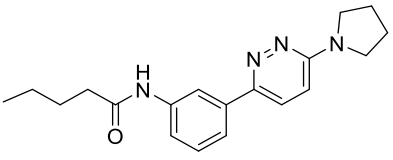
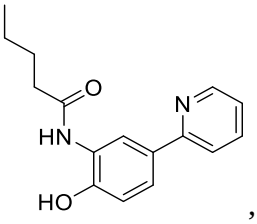
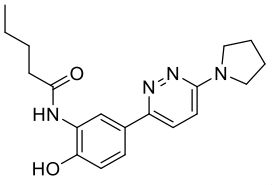
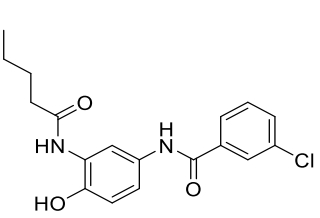
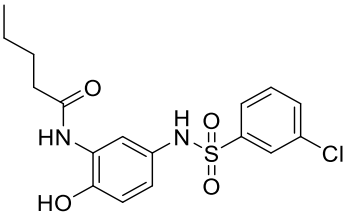
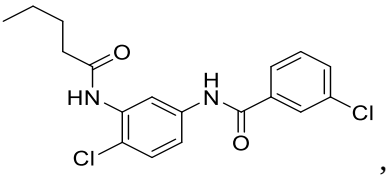
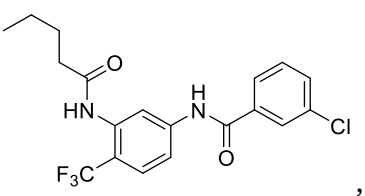
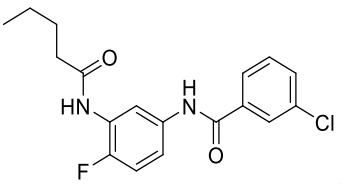
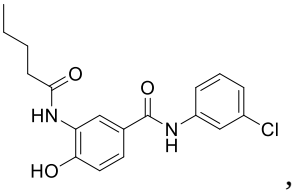
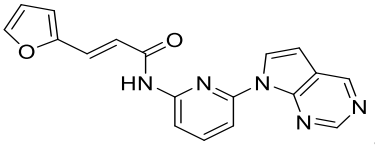
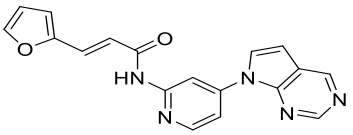
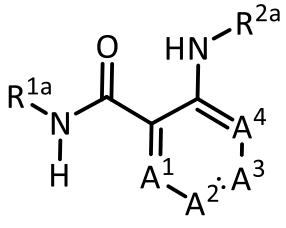
 ,  ,  ,  ,  ,  , and  , or a pharmaceutically acceptable salt or solvate thereof.

35. A compound selected from the group consisting of

 ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,

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

36. A pharmaceutical composition, comprising an effective amount of a compound of formula (IA), or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient, wherein the compound of formula (IA) has the structure:


(IA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, -C_{1-4} alkyl, halo(C_{1-4} alkyl), -C_{1-4} alkoxy, halo(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, 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; and

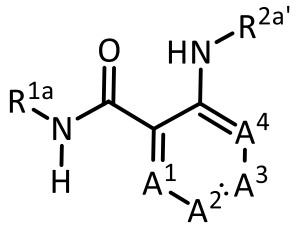
R^{2a} is selected from the group consisting of -C_{1-4} alkyl, -$C(=O)Ra^a$, -$C(=O)NHRa^a$, -$S(=O)_2Ra^a$, -C_{1-4} alkyl-$C(=O)Ra^a$, -C_{1-4} alkyl-$C(=O)NHRa^a$, -C_{1-4} alkyl-$C(=O)N(Ra^a)_2$,

-C_{1-4} alkyl-$S(=O)_2Ra^a$, -C_{1-4} alkyl-$S(=O)_2$-$N(Ra^a)_2$, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -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, –C(=O)Ra^a, -ORb^a, -SRb^a, -$N(Rb^a)_2$, (=O), -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;

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; and

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.

37. The pharmaceutical composition of claim 36, wherein the compound of formula (IA) is a compound of formula (IIA) having the structure:



(IIA),

or a pharmaceutically acceptable salt or solvate thereof, wherein

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, C_{1-4} alkyl, halo(C_{1-4} alkyl), C_{1-4} alkoxy, halo(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, 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, hydrox, -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;

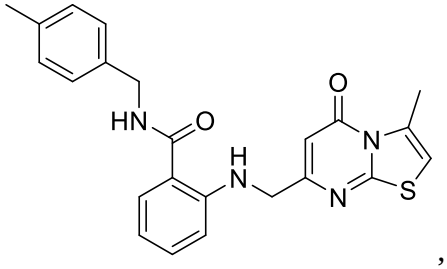
$R^{2a'}$ is selected from the group consisting of -C(=O)Ra$^{a'}$, -S(=O)$_2$Ra$^{a'}$, -C_{1-4} alkyl-C(=O)NHRa$^{a'}$, -C_{1-4} alkyl-C(=O)N(Ra$^{a'}$)$_2$, -C_{1-4} alkyl-S(=O)$_2$-N(Ra$^{a'}$)$_2$, wherein said alkyl group is optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, -CN, -C_{1-4} alkyl optionally substituted with 1, 2, or 3 halogen atoms;

Ra$^{a'}$ is selected from the group consisting of -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 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; and

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.

38. The pharmaceutical composition of claim 36, wherein the compound of formula (IA) is selected from the group consisting of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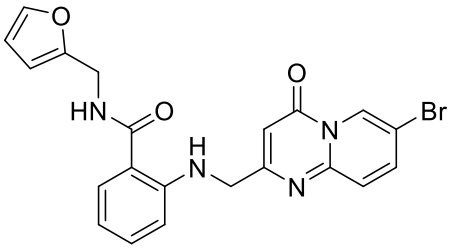
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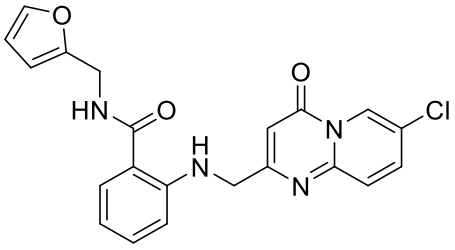
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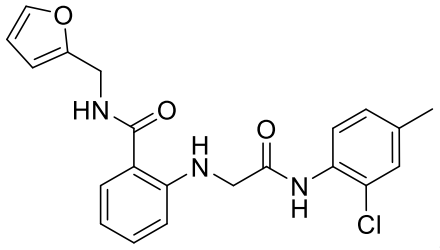
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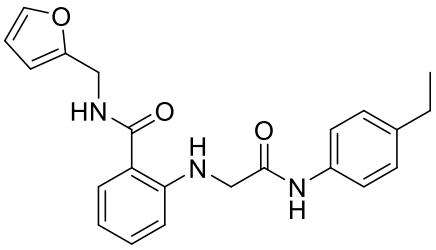
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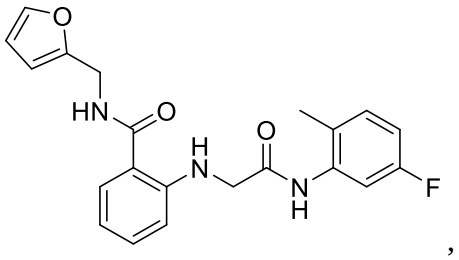
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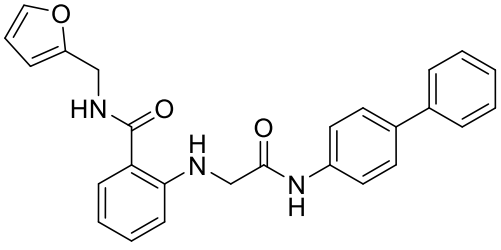
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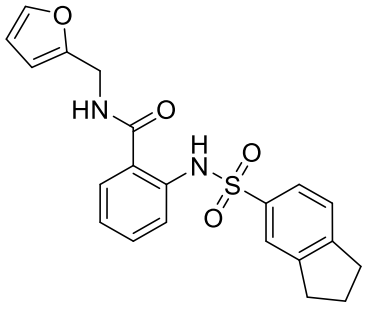
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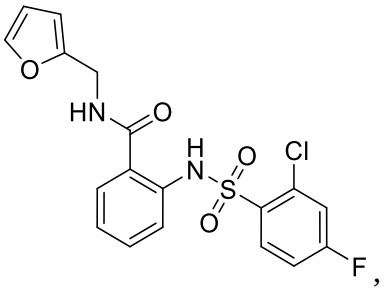
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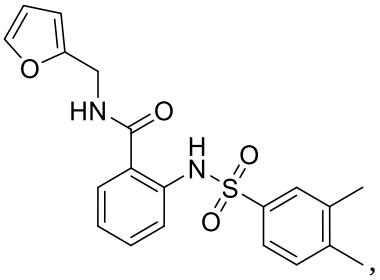
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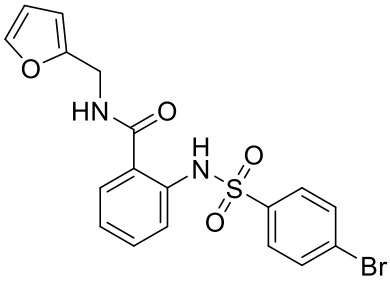
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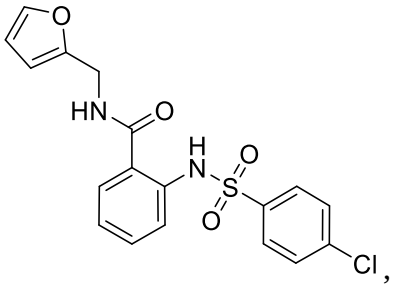
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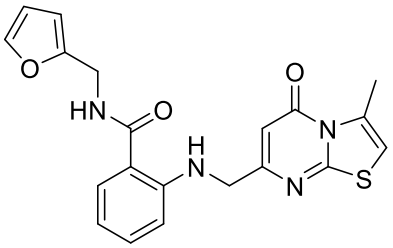
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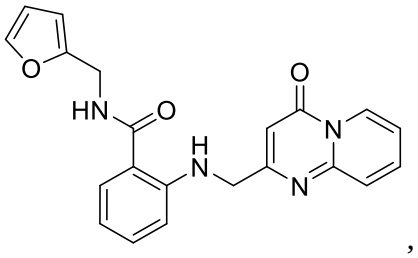
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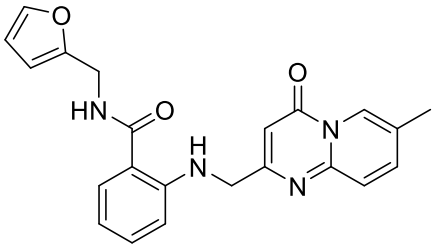
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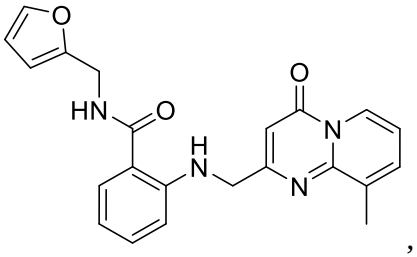
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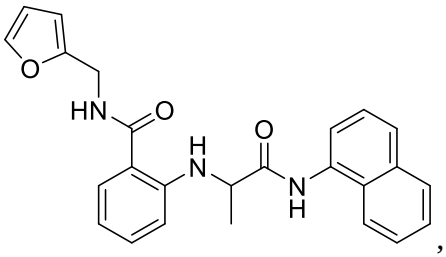
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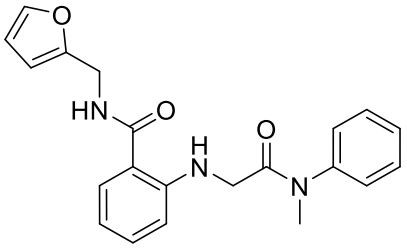
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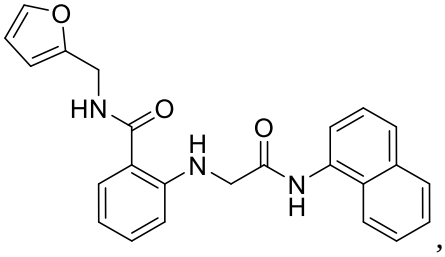
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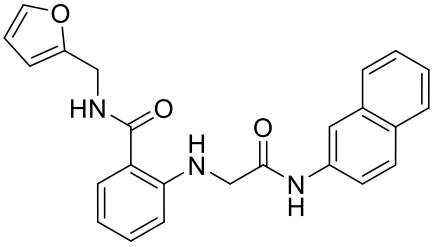
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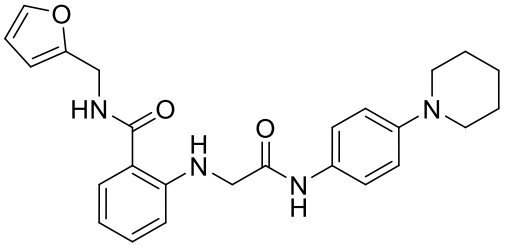
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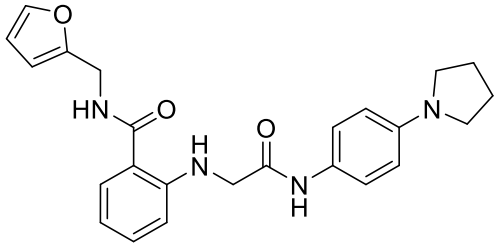
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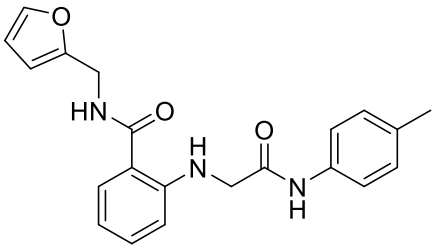
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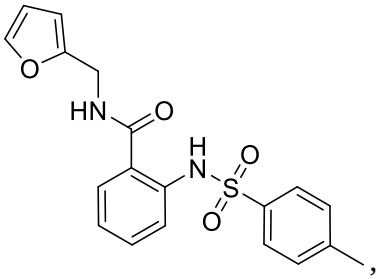
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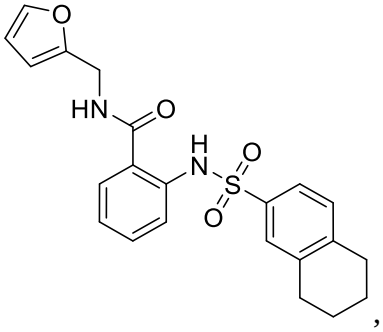
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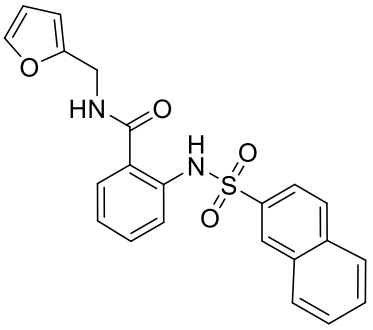
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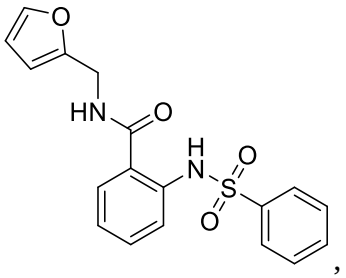
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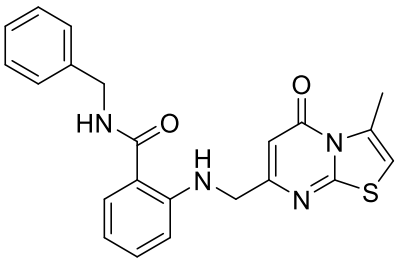
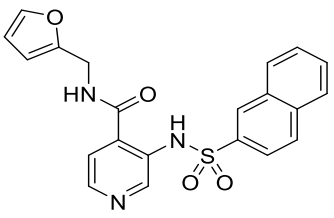

and , or a pharmaceutically acceptable salt or solvate thereof.

39. The pharmaceutical composition of claim 36, wherein the compound is selected from the group consisting of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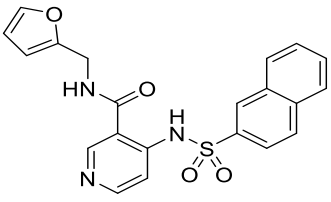
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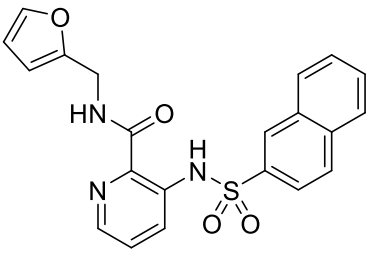
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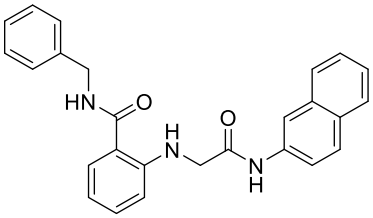
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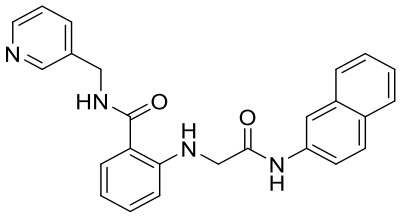
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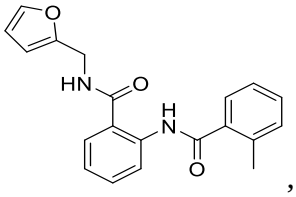
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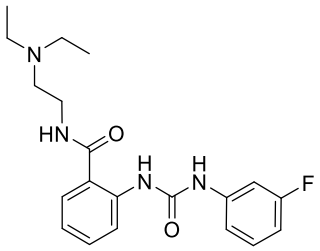
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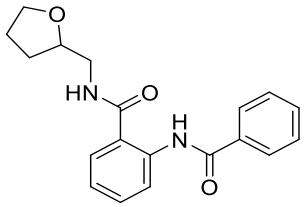
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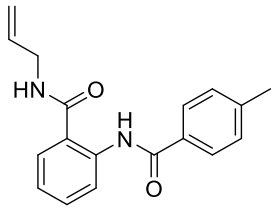
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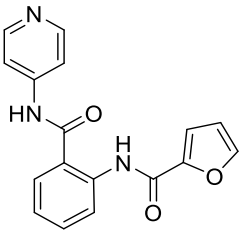
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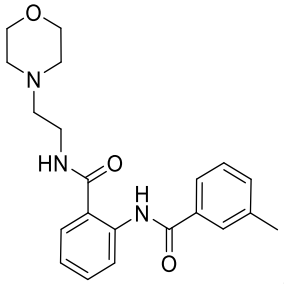
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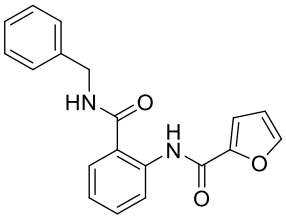
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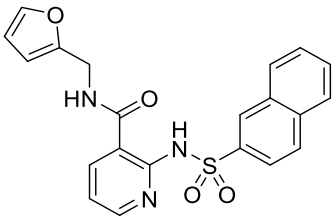
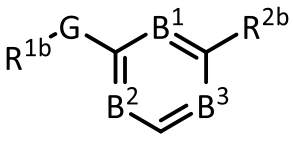

, or a pharmaceutical acceptable salt or solvate thereof.

40. A pharmaceutical composition, comprising an effective amount of a compound of formula (IB), or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient, wherein the compound of formula (IB) has the structure:


(IB),

or a pharmaceutically acceptable salt or solvate thereof, wherein

G is -C(=O)-NH- or -NH-C(=O)-;

B^1, B^2, and B^3 are each independently selected from the group consisting of N, CH and $C(R^{3b})$;

each R^{3b} is independently selected from the group consisting of halogen, C_{1-4} alkyl, halo(C_{1-4} alkyl), -OH, C_{1-4} alkoxy, halo(C_{1-4})alkoxy, and CN;

R^{1b} 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, -C_{2-4} alkylene-C_{6-10} aryl, (5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -C_{2-4} alkylene-(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_{2-4} alkenyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, alkenylheteroaryl, 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^b, -SRb^b, -$N(Rb^b)_2$, -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, alkenylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

R^{2b} is -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -C(=O)-NH-Ra^b, -$S(=O)_2$-NH-Ra^b, -C_{1-4} alkyl-$C(=O)Ra^b$, -C_{1-4} alkyl-$S(=O)_2Ra^b$, or -$N(Rb^b)_2$, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, (=O), -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently selected from the group consisting of halogen, CN, -ORb^b, and -$N(Rb^b)_2$, 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 -C_{3-10} cycloalkyl; and wherein said aryl, heteroaryl, and heterocyclyl are optionally fused to a further (second) ring; or

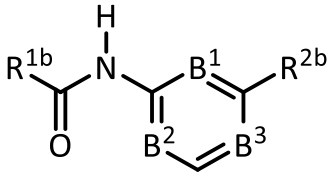
R^{2b} and R^{3b} attached to an adjacent carbon atom together form a 5- or 6-membered heterocyclic ring containing one N-atom substituted with -$S(=O)_2Ra^b$;

Ra^b 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^b, -SRb^b, -N(Rb^b)$_2$, -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; and

each Rb^b is independently hydrogen, -C(=O)Ra^b, -S(=O)$_2$Ra^b, -C$_{1-4}$ alkyl, -C$_{3-10}$ cycloalkyl, -(5- to 10-membered)-C$_{2-9}$ heterocyclyl, or optionally substituted -C$_{6-10}$ aryl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms.

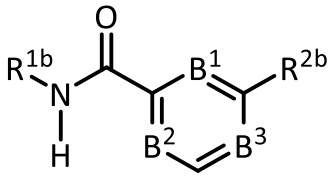
41. The pharmaceutical composition of claim 40, comprising an effective amount of a compound of formula (IB) where G is -C(=O)-NH-, which is a compound of formula (IIB):



(IIB),

or a pharmaceutically acceptable salt or solvate thereof, wherein B^1, B^2, B^3, R^{1b}, and R^{2b} are as defined in claim 40.

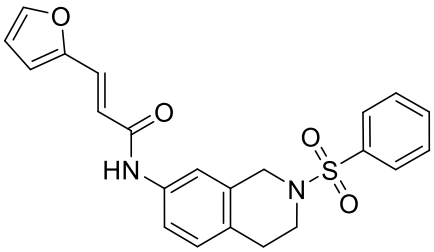
42. The pharmaceutical composition of claim 40, comprising an effective amount of a compound of formula (IB) where G is -NH-C(=O)-, which is a compound of formula (IIIB):



(IIIB),

or a pharmaceutically acceptable salt or solvate thereof, wherein B^1, B^2, B^3, R^{1b}, and R^{2b} are as defined in claim 40.

43. The pharmaceutical composition of claim 40 or 41, wherein the compound is selected from the group consisting of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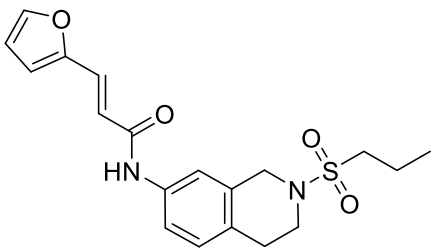
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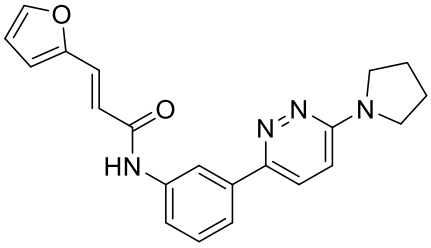
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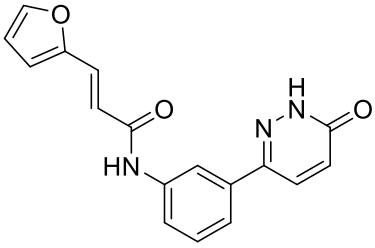
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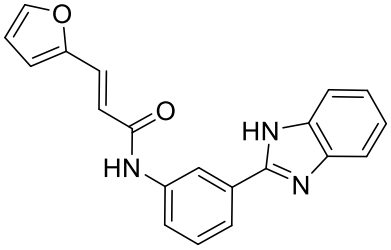
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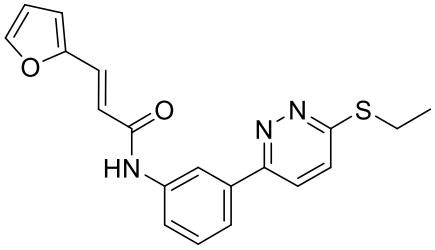
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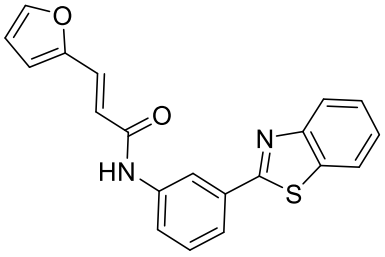
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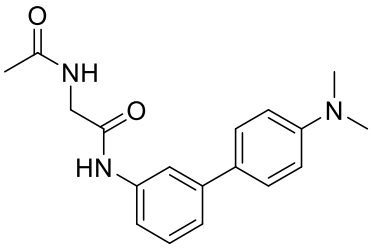
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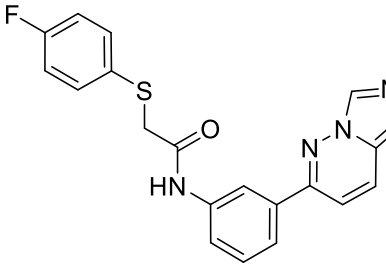
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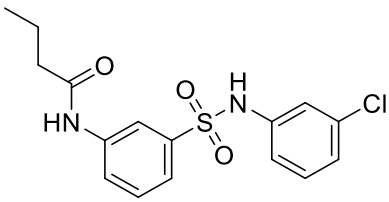
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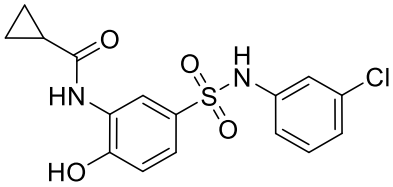
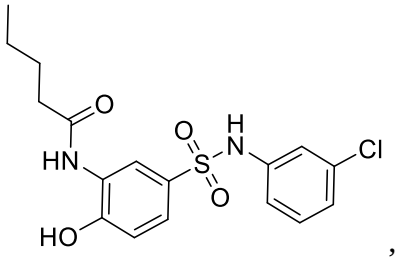
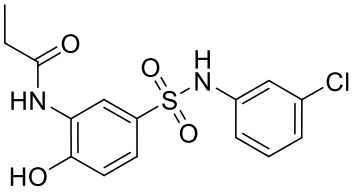
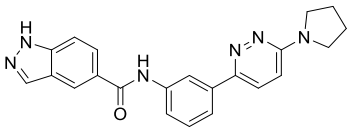
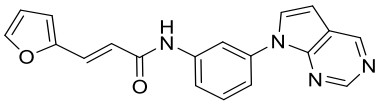
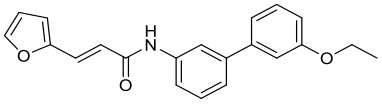
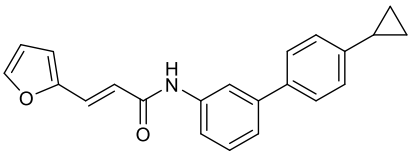
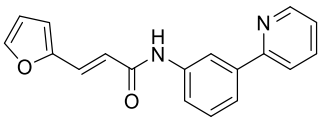
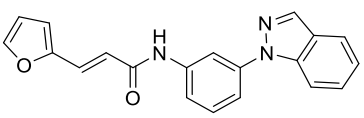
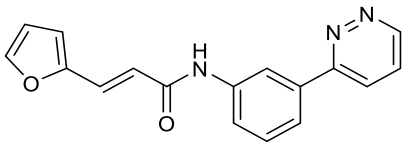
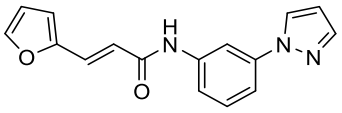
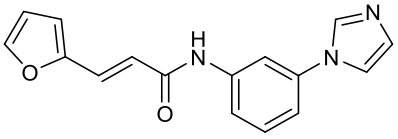
 ,  ,

 ,

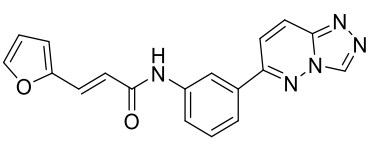
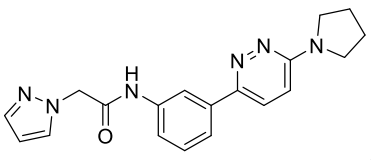
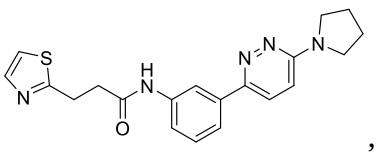
 ,  ,

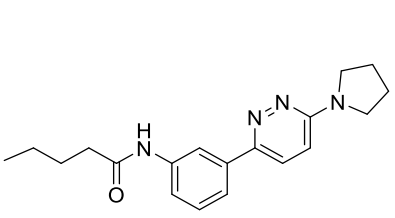
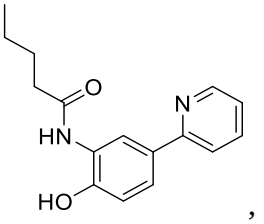
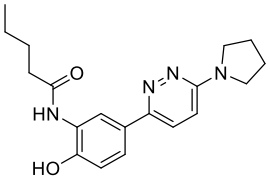
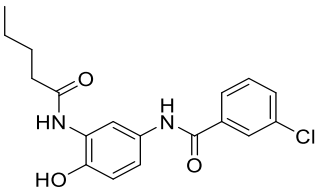
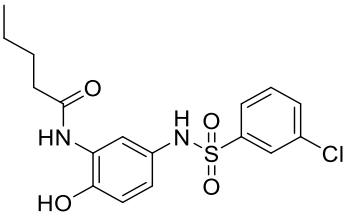
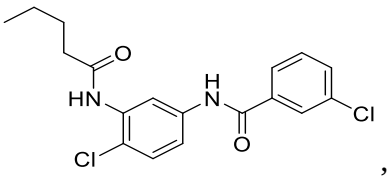
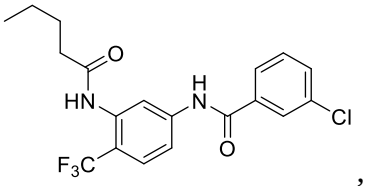
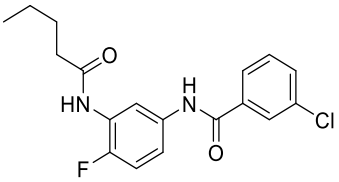
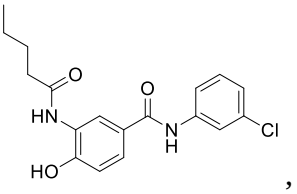
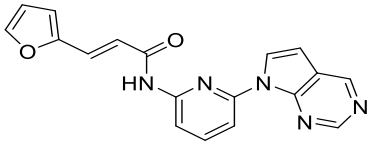
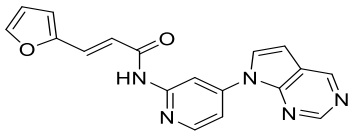
 ,  ,

 ,  ,  ,

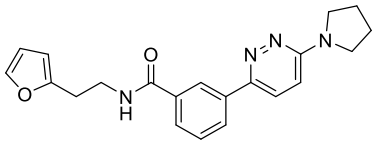
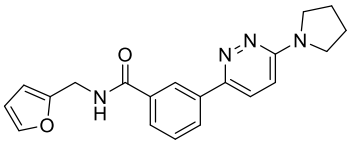
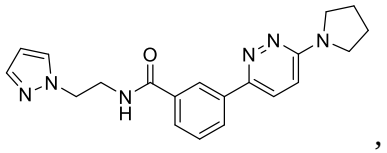
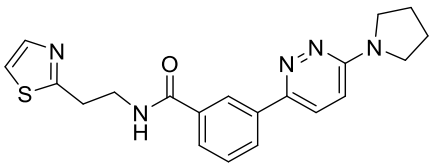
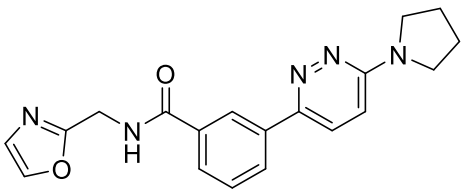
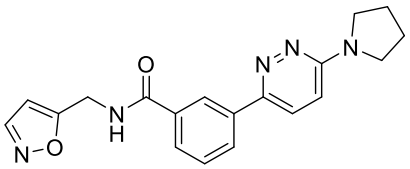
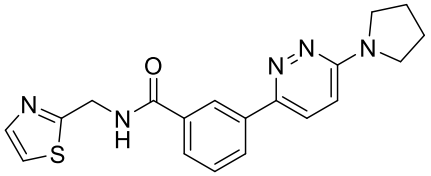
 , and  , or a pharmaceutically acceptable salt or solvate thereof.

44. The pharmaceutical composition of claim 40 or 41, wherein the compound is selected form the group consisting of

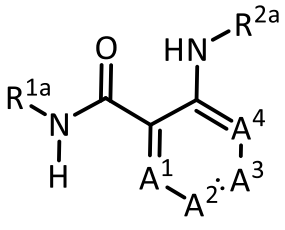
 ,  ,  ,

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

45. The pharmaceutical composition of claim 40 or 42, wherein the compound is selected from the group consisting of

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

46. A compound of formula (IA):



(IA),

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

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

each R^{3a} is independently selected from the group consisting of halogen, -OH, -C_{1-4} alkyl, halo(C_{1-4} alkyl), -C_{1-4} alkoxy, halo(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, 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; and

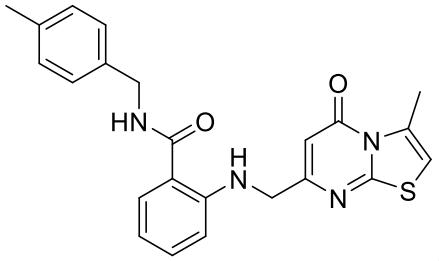
R^{2a} is selected from the group consisting of -C_{1-4} alkyl, -$C(=O)Ra^a$, -$C(=O)NHRa^a$, -$S(=O)_2Ra^a$, -C_{1-4} alkyl-$C(=O)Ra^a$, -C_{1-4} alkyl-$C(=O)NHRa^a$, -C_{1-4} alkyl-$C(=O)N(Ra^a)_2$, -C_{1-4} alkyl-$S(=O)_2Ra^a$, -C_{1-4} alkyl-$S(=O)_2$-$N(Ra^a)_2$, -C_{1-4} alkyl-C_{3-10} cycloalkyl, -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, –$C(=O)Ra^a$, -ORb^a, -SRb^a, -$N(Rb^a)_2$, (=O), -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;

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; and

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.

47. The compound for use according to claim 46, wherein the compound is selected from the group consisting of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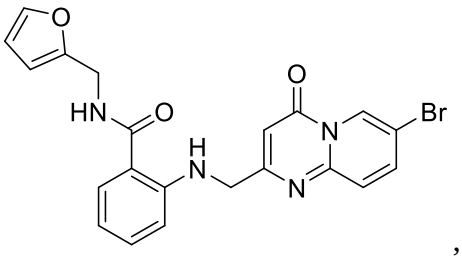
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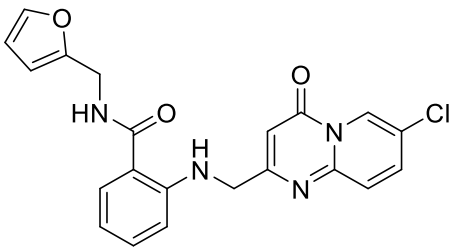
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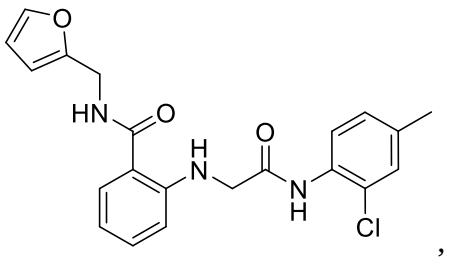
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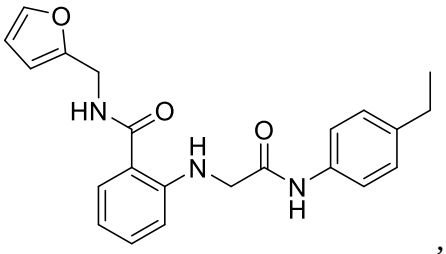
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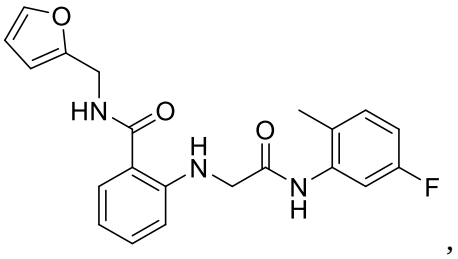
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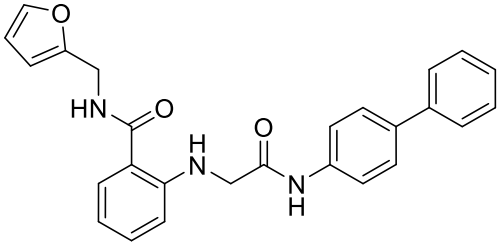
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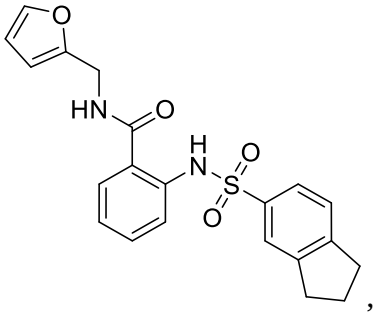
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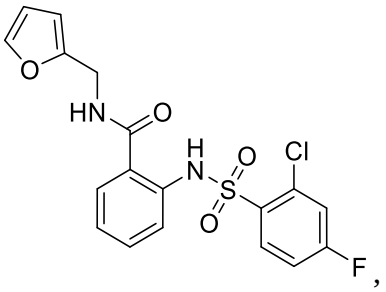
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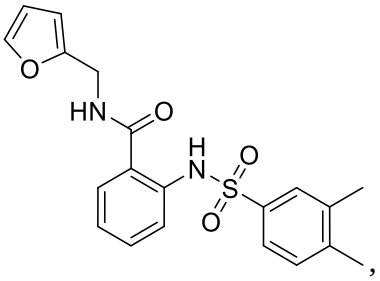
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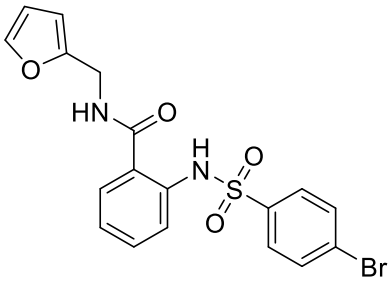
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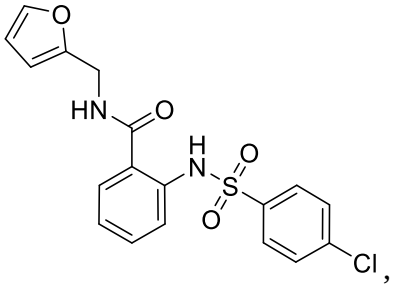
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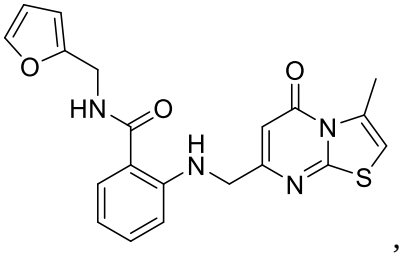
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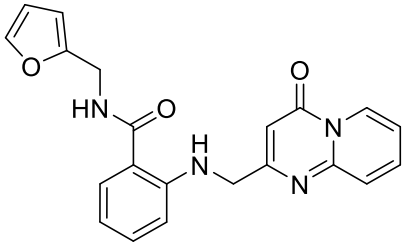
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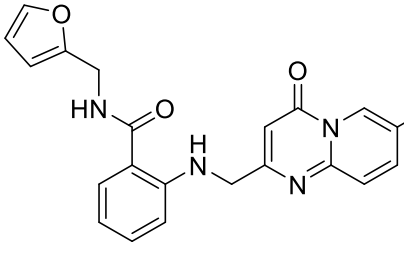
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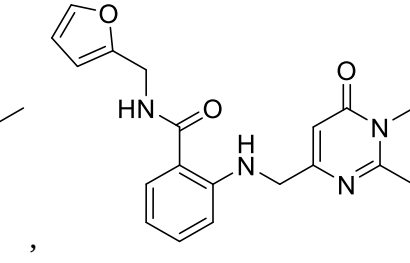
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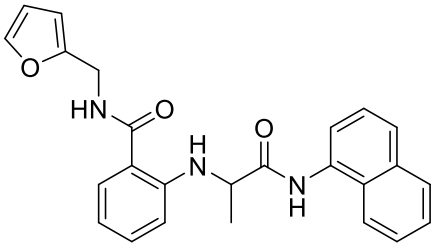
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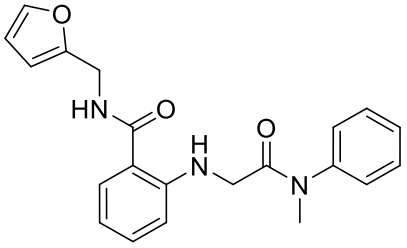
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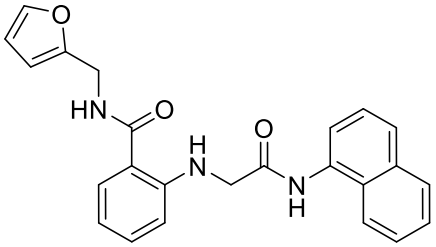
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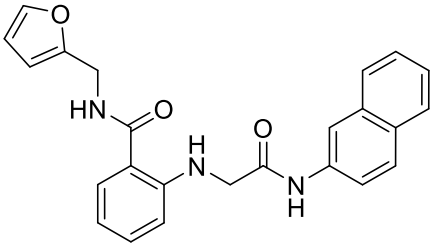
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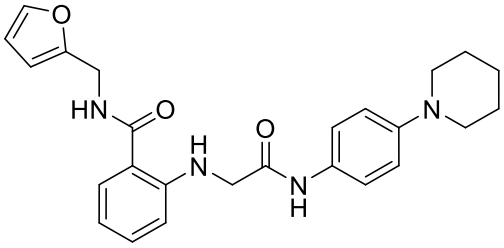
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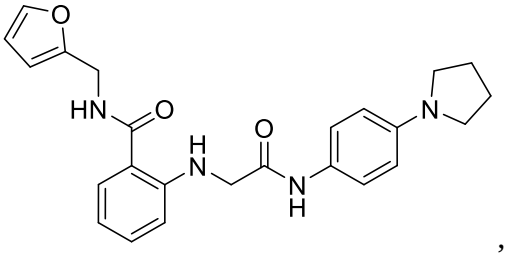
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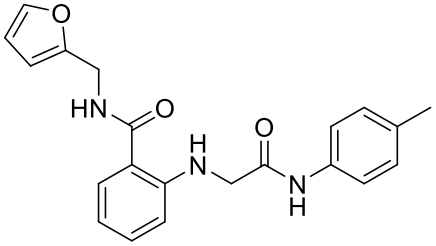
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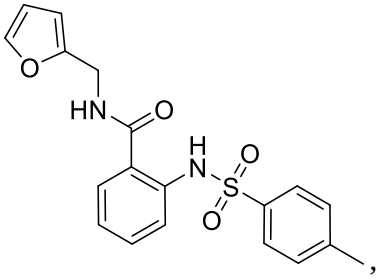
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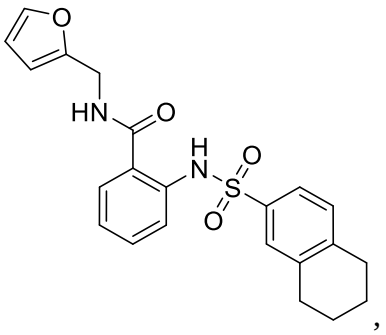
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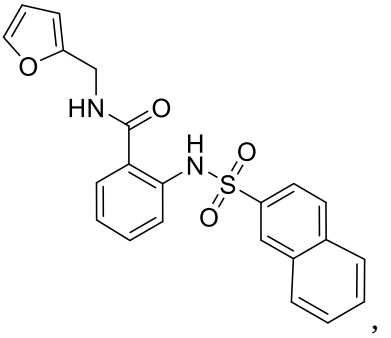
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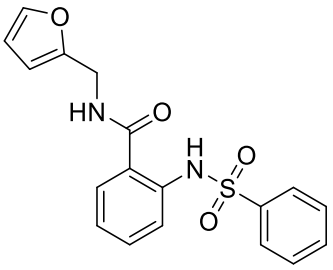
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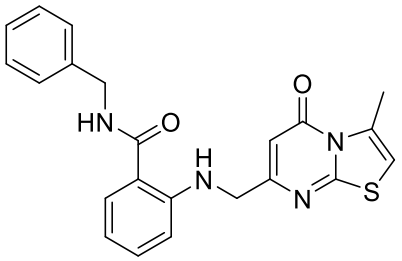
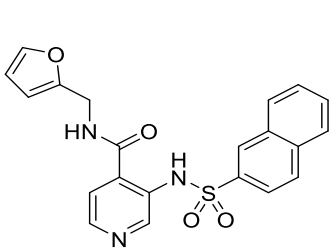


and , or a pharmaceutically acceptable salt or solvate thereof.

48. The compound for use according to claim 46, wherein the compound is selected from the group consisting of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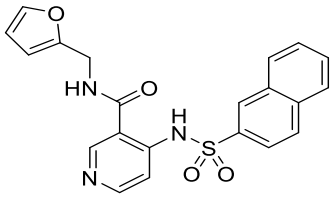
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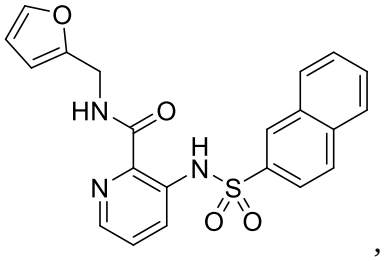
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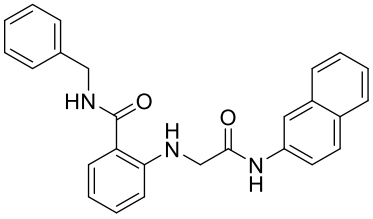
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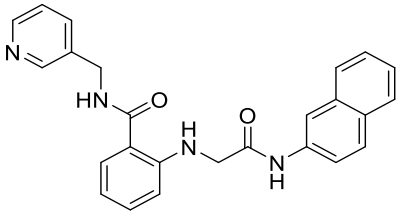
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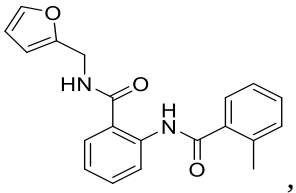
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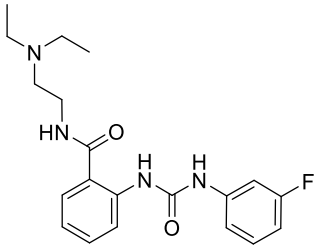
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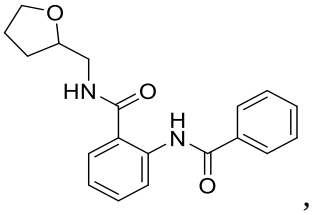
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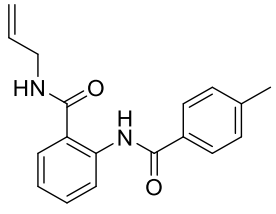
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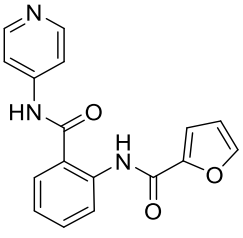
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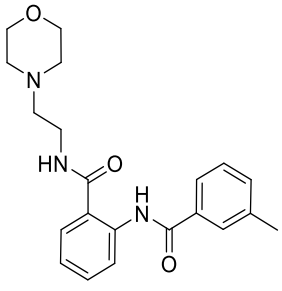
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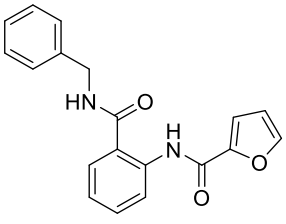
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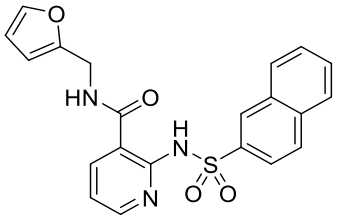
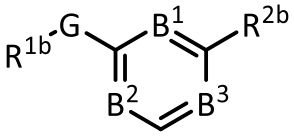


, or a pharmaceutically acceptable salt of solvate thereof.

49. A compound of formula (IB) having the structure:



(IB),

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

G is -C(=O)-NH- or -NH-C(=O)-;

B^1, B^2, and B^3 are each independently selected from the group consisting of N, CH and $C(R^{3b})$;

each R^{3b} is independently selected from the group consisting of halogen, C_{1-4} alkyl, halo(C_{1-4} alkyl), -OH, C_{1-4} alkoxy, halo(C_{1-4} alkoxy), and CN;

R^{1b} 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, -C_{2-4} alkylene-C_{6-10} aryl, (5- to 10-membered)-C_{1-9} heteroaryl, -C_{1-4} alkyl-(5- to 10-membered)-C_{1-9} heteroaryl, -C_{2-4} alkylene-(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_{2-4} alkenyl-(5- to 10-membered)-C_{2-9} heterocyclyl, wherein said alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, alkenylheteroaryl, 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^b, -SRb^b, -$N(Rb^b)_2$, -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, alkenylheteroaryl, heterocyclyl and alkylheterocyclyl is optionally fused to a further (second) ring;

R^{2b} is -C_{6-10} aryl, -(5- to 10-membered)-C_{1-9} heteroaryl, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -$C(=O)$-NH-Ra^b, -$S(=O)_2$-NH-Ra^b, -C_{1-4} alkyl-$C(=O)Ra^b$, -C_{1-4} alkyl-$S(=O)_2Ra^b$, or

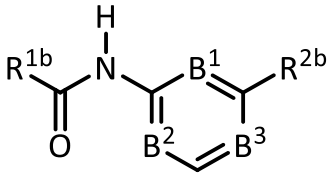
-$N(Rb^b)_2$, wherein said aryl and heteroaryl groups are optionally substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, hydroxy, CN, -ORb^b, -SRb^b, -$N(Rb^b)_2$, (=O), -C_{1-4}alkyl optionally substituted with 1, 2, or 3 substituents each independently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

R^{2b} and R^{3b} attached to an adjacent carbon atom together form a 5- or 6-membered heterocyclic ring containing one N-atom substituted with -$S(=O)_2Ra^b$;

Ra^b 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^b, -SRb^b, -$N(Rb^b)_2$, -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; and

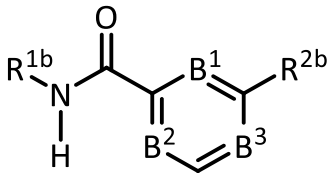
each Rb^b is independently hydrogen, -$C(=O)Ra^b$, -$S(=O)_2Ra^b$, -C_{1-4} alkyl, -C_{3-10} cycloalkyl, -(5- to 10-membered)-C_{2-9} heterocyclyl, or optionally substituted -C_{6-10} aryl, wherein said alkyl, cycloalkyl or heterocyclyl group is optionally substituted by 1, 2 or 3 fluorine atoms.

50. The compound for use according to claim 49, which is compound of formula (IIB):



(IIB), or

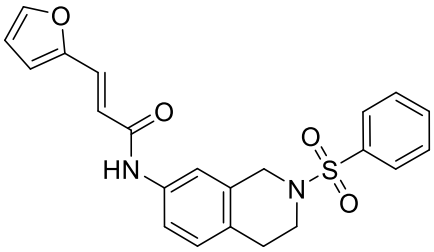
a compound of formula (IIIB):



(IIIB),

or a pharmaceutically acceptable salt or solvate thereof, wherein B^1, B^2, B^3, R^{1b}, and R^{2b} are as defined in claim 49.

51. The compound for use according to claim 49 or 50, wherein the compound is selected from the group consisting of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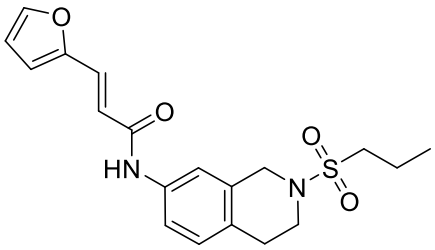
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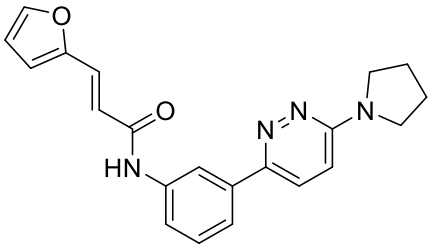
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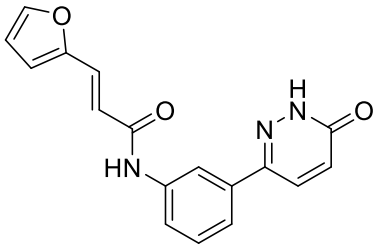
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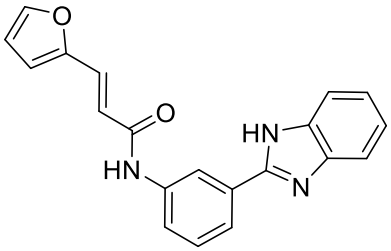
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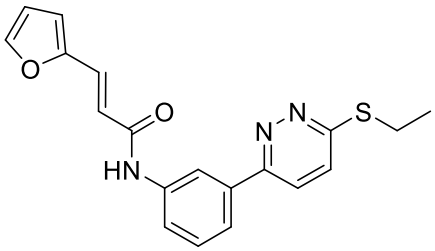
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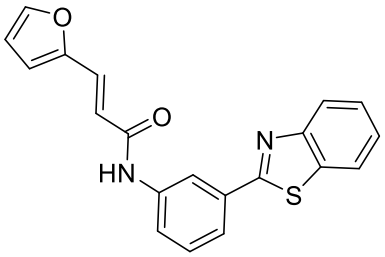
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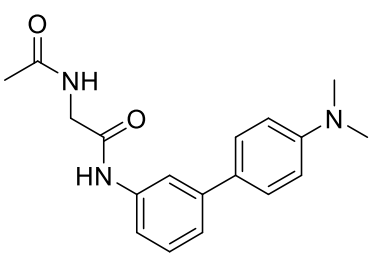
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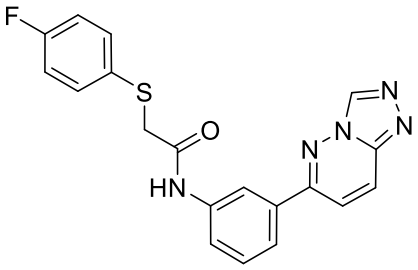
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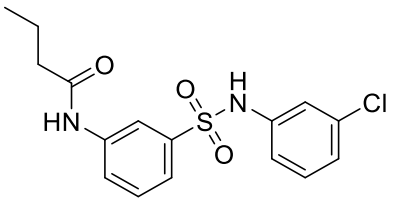
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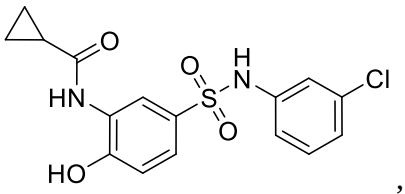
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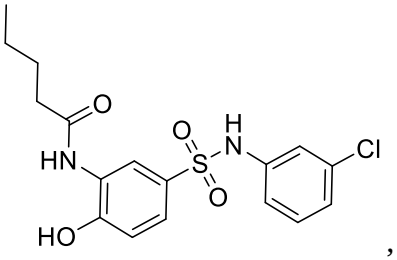
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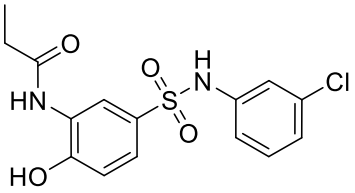
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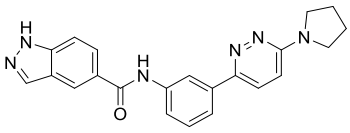
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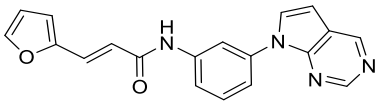
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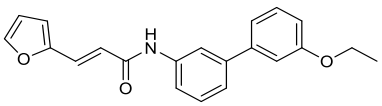
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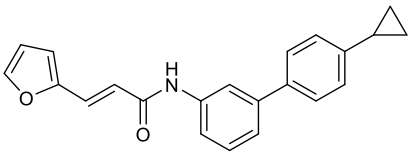
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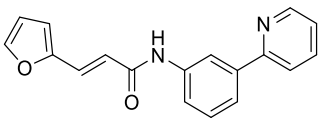
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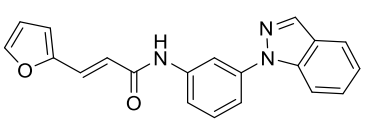
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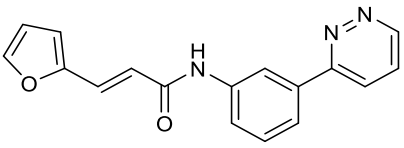
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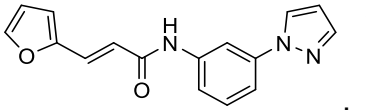
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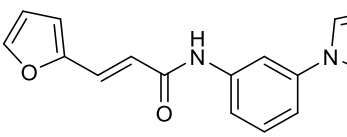
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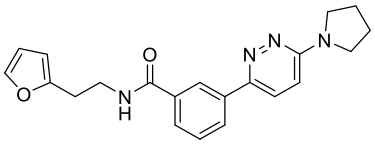
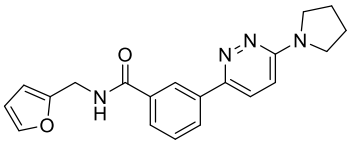
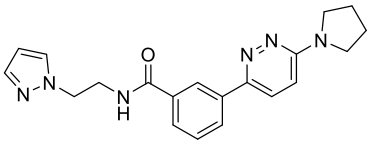
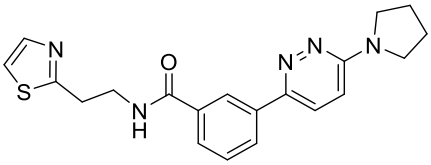
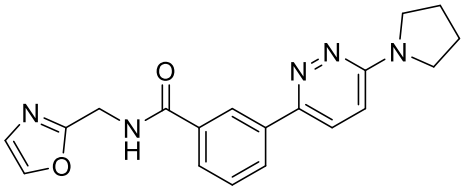
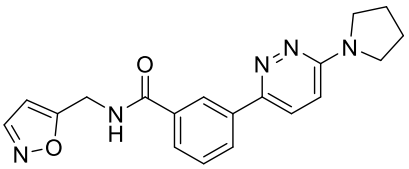
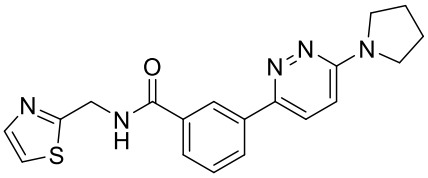
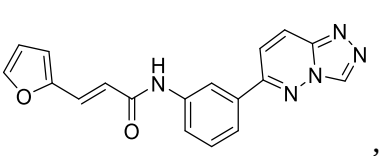
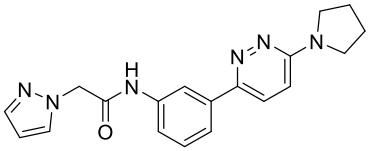
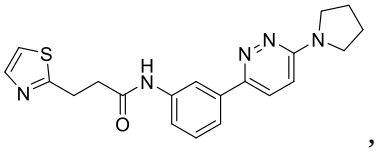
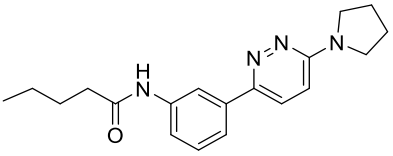
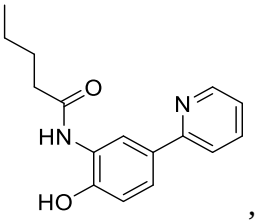
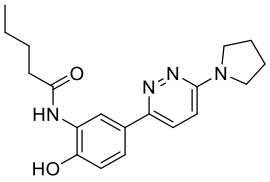
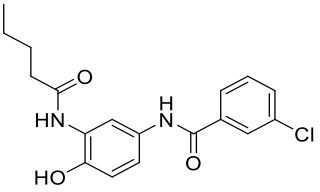
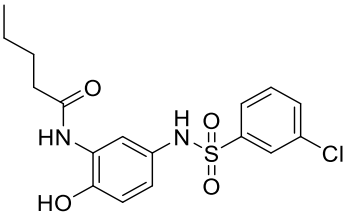
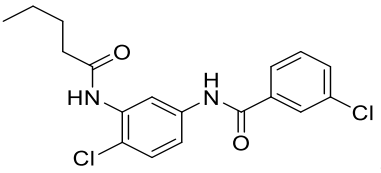
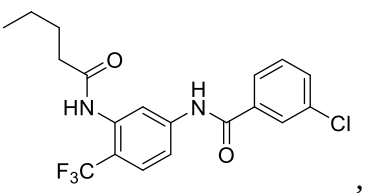
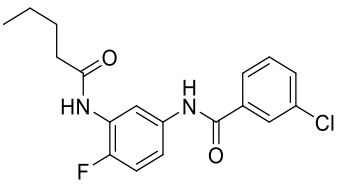
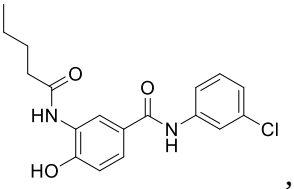
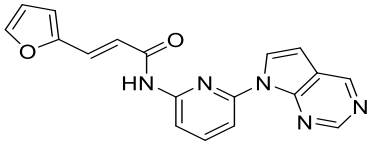
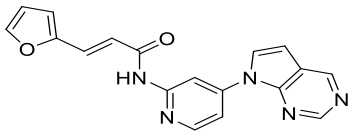
 ,  ,  ,  ,  ,  , and  or a pharmaceutically acceptable salt or solvate thereof.

52. The compound for use according to claim 49 or 50, wherein the compound is selected from the group consisting of

 ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,



, and 

, or a pharmaceutically acceptable salt or solvate thereof.

53. The compound for use according to any one of claims 49-52, wherein the medicament is for use in the treatment or prevention of a lysosomal storage disease, an α-synucleinopathy, or a disease or disorder selected from the group consisting of Krabbe's disease, demyelinating disorders, galactosylsphingosine related disorders, globoid cell leukodystrophy, multiple sclerosis (MS), Parkinson’s disease, peripheral neuropathy, progressive multiple sclerosis, pulmonary artery enlargement in COPD, open angle glaucoma, Lewy body dementia, and multiple system atrophy (MSA).