- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazole;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{2-6}$-alkenyl, $C_{2-6}$-alkynyl, $C_{1-6}$-haloalkyl, $C_{1-6}$-alkylene-OH, $C_{2-6}$-alkenylene-OH, $C_{2-6}$-alkynylene-OH, $CH_2CON(C_{1-6}\text{-alkyl})_2$, $CH_2NHCONH\text{-}C_{3-6}$-cycloalkyl, CN, CO-pyridinyl, $CONR^{1.1.1}R^{1.1.2}$, $COO\text{-}C_{1-6}$-alkyl, $N(SO_2\text{-}C_{1-6}\text{-alkyl})(CH_2CON(C_{1-4}\text{-alkyl})_2)$ $O\text{-}C_{1-6}$-alkyl, O-pyridinyl, $SO_2\text{-}C_{1-6}$-alkyl, $SO_2\text{-}C_{1-6}$-alkylen-OH, $SO_2\text{-}C_{3-6}$-cycloalkyl, $SO_2$-piperidinyl, $SO_2NH\text{-}C_{1-6}$-alkyl, $SO_2N(C_{1-6}\text{-alkyl})_2$, halogen, CN, CO-morpholinyl, $CH_2$-pyridinyl or a heterocyclic ring optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $NHC_{1-6}$-alkyl and =O;

$R^{1.1.1}$ H, $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, $C_{1-6}$-haloalkyl, $CH_2CON(C_{1-6}\text{-alkyl},)_2$, $CH_2CO$-azetindinyl, $C_{1-6}$-alkylen-$C_{3-6}$-cycloalkyl, $CH_2$-pyranyl, $CH_2$-tetrahydrofuranyl, $CH_2$-furanyl, $C_{1-6}$-alkylen-OH or thiadiazolyl, optionally substituted with $C_{1-6}$-alkyl;

$R^{1.1.2}$ H, $C_{1-6}$-alkyl, $SO_2C_{1-6}$-alkyl;

or $R^{1.1.1}$ and $R^{1.1.2}$ together with the nitrogen atom of $CONR^{1.1.1}R^{1.1.2}$ are forming a four-, five- or six-membered heterocyclic ring, optionally containing one N or O, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{1-4}$-alkylene-OH, OH, =O;

or

$R^{1.1}$ is phenyl, wherein two adjacent residues are together forming a five- or six-membered carbocyclic aromatic or non-aromatic ring, optionally containing independently from each other one or two N, S, or $SO_2$, replacing a carbon atom of the ring, wherein the ring is optionally substituted with $C_{1-4}$-alkyl or =O;

$R^{1.2}$ is selected from

$R^{1.3}$ is selected from phenyl, heteroaryl or indolyl, each optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, O-$C_{1-6}$-alkyl, O-$C_{1-6}$-haloalkyl, phenyl, heteroaryl;

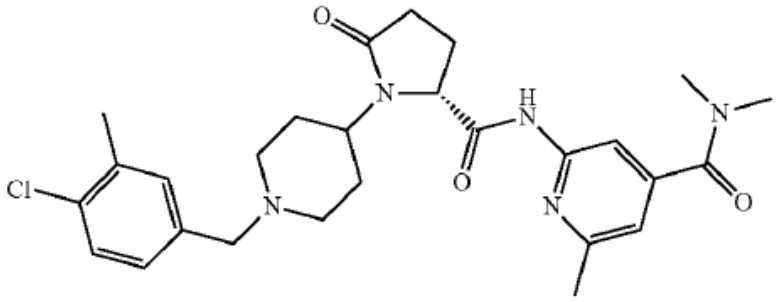
**$R^2$** is selected from the group consisting of $C_{1-6}$-alkylene-phenyl, $C_{1-6}$-alkylene-naphthyl, and $C_{1-6}$-alkylene-heteroaryl; each optionally substituted with one, two or three residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{1-6}$-haloalkyl, O-$C_{1-6}$-alkyl, O-$C_{1-6}$-haloalkyl, halogen;

**$R^3$** is H, $C_{1-6}$-alkyl;

**$R^4$** is H, $C_{1-6}$-alkyl;

or **$R^3$** and **$R^4$** together are forming a $CH_2$-$CH_2$ group.

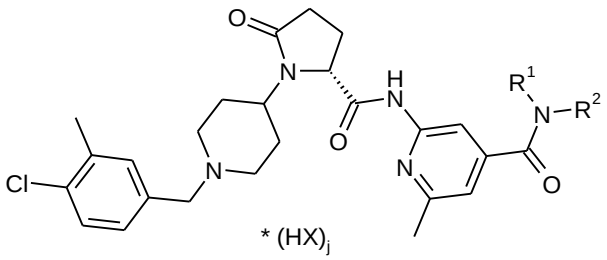
In another aspect, the present disclosure provides use of a crystalline salt of a compound of the formula below in the manufacture of a medicament for treating aging-associated neuronal loss, memory impairment, or loss of motor coordination in a subject diagnosed with the aging-associated neuronal loss, memory impairment, or loss of motor coordination, wherein the medicament is to be administered in the subject




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In another aspect, the present disclosure provides use of a pharmaceutical composition comprising at least one co-crystal of the crystalline salt of the compound as defined herein and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating aging-associated neuronal loss, memory impairment, or loss of motor coordination in a subject, wherein the pharmaceutical composition is to be administered in the subject .

In another aspect, the present disclosure provides use of a pharmaceutical composition comprising a compound of formula 3 in the manufacture of a medicament for treating aging-associated neuronal loss, memory impairment, or loss of motor coordination in a subject, wherein the compound of formula 3 is to be administered in the subject and has the following formula:




3

wherein

$R^1$ is H, $C_{1-6}$-alkyl, $C_{0-4}$-alkyl-$C_{3-6}$-cycloalkyl, $C_{1-6}$-haloalkyl;

$R^2$ is H, $C_{1-6}$-alkyl;

X is an anion selected from the group consisting of chloride or ½ dibenzoyltartrate

j is 1 or 2,

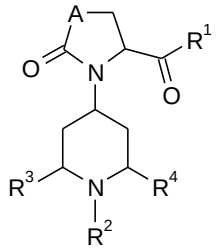
and the pharmaceutical composition further comprises a first diluent, a second diluent, a binder, a disintegrant and a lubricant.

## IV. Incorporation by Reference

Claims

What is claimed:

1. Use of a compound of formula 1 in the manufacture of a medicament for treating aging-associated neuronal loss, memory impairment, or loss of motor coordination in a subject diagnosed with the aging-associated neuronal loss, memory impairment, or loss of motor coordination, wherein the compound of formula 1 is to be administered in the subject and has the following formula:




1

wherein

A is $CH_2$, O or N-$C_{1-6}$-alkyl;

$R^1$ is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-$C_{3-6}$-cycloalkyl, whereas optionally one carbon atom is replaced by a nitrogen atom, whereas the ring is optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, O-$C_{1-6}$-alkyl, $NHSO_2$-phenyl, NHCONH-phenyl, halogen, CN, $SO_2$-$C_{1-6}$-alkyl, COO-$C_{1-6}$-alkyl;
- a $C_{9 \text{ or } 10}$-bicyclic-ring, whereas one or two carbon atoms are replaced by nitrogen atoms and the ring system is bound via a nitrogen atom to the basic structure of formula 1 and whereas the ring system is optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, COO-$C_{1-6}$-alkyl, $C_{1-6}$-haloalkyl, O-$C_{1-6}$-alkyl, $NO_2$, halogen, CN, $NHSO_2$-$C_{1-6}$-alkyl, methoxy-phenyl;

- a group selected from NHCH(pyridinyl)$CH_2COO$-$C_{1-6}$-alkyl, NHCH($CH_2O$-$C_{1-6}$-alkyl)-benzoimidazolyl, optionally substituted with halogen or CN;
- piperidinyl, optionally substituted with one or two residues selected from the group consisting of $NHSO_2$-$C_{1-4}$-alkyl, m-methoxyphenyl;
- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazole;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{2-6}$-alkenyl, $C_{2-6}$-alkynyl, $C_{1-6}$-haloalkyl, $C_{1-6}$-alkylene-OH, $C_{2-6}$-alkenylene-OH, $C_{2-6}$-alkynylene-OH, $CH_2CON(C_{1-6}\text{-alkyl})_2$, $CH_2NHCONH$-$C_{3-6}$-cycloalkyl, CN, CO-pyridinyl, $CONR^{1.1.1}R^{1.1.2}$, $COO$-$C_{1-6}$-alkyl, $N(SO_2\text{-}C_{1-6}\text{-alkyl})(CH_2CON(C_{1-4}\text{-alkyl})_2)$ O-$C_{1-6}$-alkyl, O-pyridinyl, $SO_2$-$C_{1-6}$-alkyl, $SO_2$-$C_{1-6}$-alkylen-OH, $SO_2$-$C_{3-6}$-cycloalkyl, $SO_2$-piperidinyl, $SO_2NH$-$C_{1-6}$-alkyl, $SO_2N(C_{1-6}\text{-alkyl})_2$, halogen, CN, CO-morpholinyl, $CH_2$-pyridinyl or a heterocyclic ring optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $NHC_{1-6}$-alkyl and =O;

$R^{1.1.1}$ H, $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, $C_{1-6}$-haloalkyl, $CH_2CON(C_{1-6}\text{-alkyl},)_2$, $CH_2CO$-azetindinyl, $C_{1-6}$-alkylen-$C_{3-6}$-cycloalkyl, $CH_2$-pyranyl, $CH_2$-tetrahydrofuranyl, $CH_2$-furanyl, $C_{1-6}$-alkylen-OH or thiadiazolyl, optionally substituted with $C_{1-6}$-alkyl;

$R^{1.1.2}$ H, $C_{1-6}$-alkyl, $SO_2C_{1-6}$-alkyl;

or $R^{1.1.1}$ and $R^{1.1.2}$ together with the nitrogen atom of $CONR^{1.1.1}R^{1.1.2}$ are forming a four-, five- or six-membered heterocyclic ring, optionally containing one N or O, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{1-4}$-alkylene-OH, OH, =O;

or

$R^{1.1}$ is phenyl, wherein two adjacent residues are together forming a five- or six-membered carbocyclic aromatic or non-aromatic ring, optionally containing independently from each other one or two N, S, or $SO_2$, replacing a carbon atom of the ring, wherein the ring is optionally substituted with $C_{1-4}$-alkyl or =O;

$R^{1.2}$ is selected from

- heteroaryl, optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{2-6}$-alkenyl, $C_{2-6}$-alkynyl, $C_{3-6}$-cycloalkyl, $CH_2COO$-$C_{1-6}$-alkyl, $CONR^{1.2.1}R^{1.2.2}$, $COR^{1.2.3}$, $COO$-$C_{1-6}$-alkyl, $CONH_2$, O-$C_{1-6}$-alkyl, halogen, CN, $SO_2N(C_{1-6}\text{-alkyl})_2$ or heteroaryl optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl;
- heteroaryl, optionally substituted with a five- or six-membered carbocyclic non-aromatic ring containing independently from each other two N, O, S, or $SO_2$, replacing a carbon atom of the ring;
- an aromatic or non-aromatic $C_{9\text{ or }10}$-bicyclic-ring, whereas one or two carbon atoms are replaced by N, O or S each optionally substituted with one or two residues selected from the group consisting of $N(C_{1-6}\text{-alkyl})_2$, CONH-$C_{1-6}$-alkyl, =O;
- a heterocyclic non-aromatic ring, optionally substituted with pyridinyl;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with NHCO-$C_{1-6}$-alkyl,

$R^{1.2.1}$ H, $C_{1-6}$-alkyl, $C_{1-6}$-alkylene-$C_{3-6}$-cycloalkyl, $C_{1-4}$-alkylene-phenyl, $C_{1-4}$-alkylene-furanyl, $C_{3-6}$-cycloalkyl, $C_{1-4}$-alkylene-O-$C_{1-4}$-alkyl, $C_{1-6}$-haloalkyl or a five- or six-membered carbocyclic non-aromatic ring, optionally containing independently from each other one or two N, O, S, or $SO_2$, replacing a carbon atom of the ring, optionally substituted with 4-cyclopropylmethyl-piperazinyl

$R^{1.2.2}$ H, $C_{1-6}$-alkyl;

$R^{1.2.3}$ a five- or six-membered carbocyclic non-aromatic ring, optionally containing independently from each other one or two N, O, S, or $SO_2$, replacing a carbon atom of the ring;

$R^{1.3}$ is selected from phenyl, heteroaryl or indolyl, each optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, O-$C_{1-6}$-alkyl, O-$C_{1-6}$-haloalkyl, phenyl, heteroaryl;

$R^2$ is selected from the group consisting of $C_{1-6}$-alkylene-phenyl, $C_{1-6}$-alkylene-naphthyl, and $C_{1-6}$-alkylene-heteroaryl; each optionally substituted with one, two or three residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{1-6}$-haloalkyl, O-$C_{1-6}$-alkyl, O-$C_{1-6}$-haloalkyl, halogen;

$R^3$ is H, $C_{1-6}$-alkyl;

$R^4$ is H, $C_{1-6}$-alkyl;

or $R^3$ and $R^4$ together are forming a $CH_2$-$CH_2$ group.

2. The use of claim 1 wherein the compound of formula 1,

A is $CH_2$, O or N-$C_{1-4}$-alkyl;

$R^1$ is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-$C_{3-6}$-cycloalkyl, whereas optionally one carbon atom is replaced by a nitrogen atom, whereas the ring is optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, O-$C_{1-6}$-alkyl, $NHSO_2$-phenyl, NHCONH-phenyl, halogen, CN, $SO_2$-$C_{1-6}$-alkyl, COO-$C_{1-6}$-alkyl;

- a $C_{9 \text{ or } 10}$-bicyclic-ring, whereas one or two carbon atoms are replaced by nitrogen atoms and the ring system is bound via a nitrogen atom to the basic structure of formula 1 and whereas the ring system is optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, COO-$C_{1-6}$-alkyl, $C_{1-6}$-haloalkyl, O-$C_{1-6}$-alkyl, $NO_2$, halogen, CN, $NHSO_2$-$C_{1-6}$-alkyl, m-methoxyphenyl;
- a group selected from NHCH(pyridinyl)$CH_2$COO-$C_{1-6}$-alkyl, NHCH($CH_2$O-$C_{1-6}$-alkyl)-benzoimidazolyl, optionally substituted with Cl;
- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazolyl;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{1-6}$-haloalkyl, $CH_2CON(C_{1-6}\text{-alkyl})_2$, $CH_2NHCONH$-$C_{3-6}$-cycloalkyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COO-$C_{1-6}$-alkyl, O-$C_{1-6}$-alkyl, $SO_2$-$C_{1-6}$-alkyl, $SO_2$-$C_{1-6}$-alkylen-OH, $SO_2$-$C_{3-6}$-cycloalkyl, $SO_2$-piperidinyl, $SO_2NH$-$C_{1-6}$-alkyl, $SO_2N(C_{1-6}\text{-alkyl})_2$, halogen, CN, CO-morpholinyl, $CH_2$-pyridinyl or a heterocyclic ring optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $NHC_{1-6}$-alkyl,, =O;

$R^{1.1.1}$ H, $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, $C_{1-6}$-haloalkyl, $CH_2CON(C_{1-6}\text{-alkyl},)_2$, $CH_2CO$-azetindinyl, $C_{1-6}$-alkylen-$C_{3-6}$-cycloalkyl, $CH_2$-pyranyl, $CH_2$-tetrahydrofuranyl, $CH_2$-furanyl, $C_{1-6}$-alkylen-OH or thiadiazolyl, optionally substituted with $C_{1-6}$-alkyl;

$R^{1.1.2}$ H, $C_{1-6}$-alkyl, $SO_2C_{1-6}$-alkyl;

or $R^{1.1.1}$ and $R^{1.1.2}$ together with the nitrogen atom of $CONR^{1.1.1}R^{1.1.2}$ are forming a four-, five- or six-membered heterocyclic ring, optionally containing one O, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of $CH_2OH$

$R^{1.2}$ is selected from

- heteroaryl, optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, $CH_2COO$-$C_{1-6}$-alkyl, $CONR^{1.2.1}R^{1.2.2}$, $COO$-$C_{1-6}$-alkyl, $CONH_2$, O-$C_{1-6}$-alkyl, halogen, CN, CO-pyrrolidinyl, CO-morpholinyl or heteroaryl optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl;
- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of $N(C_{1-6}\text{-alkyl})_2$, $CONH$-$C_{1-6}$-alkyl, =O;
- piperidinyl, optionally substituted with pyridinyl;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with $NHCO$-$C_{1-6}$-alkyl,

$R^{1.2.1}$ H, $C_{1-6}$-alkyl;

$R^{1.2.2}$ H, $C_{1-6}$-alkyl;

$R^{1.3}$ is selected from phenyl, pyrazolyl, isoxazolyl, pyrimidinyl, indolyl or oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, O-$C_{1-6}$-alkyl, O-$C_{1-6}$-haloalkyl;

$R^2$ is selected from $CH_2$-phenyl or $CH_2$-naphthyl, both optionally substituted with one or two residues selected from the group consisting of $C_{1-6}$-alkyl, $C_{1-6}$-haloalkyl, O-$C_{1-6}$-alkyl, O-$C_{1-6}$-haloalkyl, halogen; or $CH_2$-thiophenyl, optionally substituted with one or two residues selected from the group consisting of halogen;

$R^3$ is H, $C_{1-4}$-alkyl;

$R^4$ is H, $C_{1-4}$-alkyl;

or $R^3$ and $R^4$ together are forming a $CH_2$-$CH_2$ group.

3. The use of claim 1 wherein the compound of formula 1 is

A is $CH_2$, O or NMe;

$R^1$ is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-cyclohexyl, optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl, $NHSO_2$-phenyl, NHCONH-phenyl, halogen;
- NH-pyrrolidinyl, optionally substituted with one or two residues selected from the group consisting of $SO_2$-$C_{1-4}$-alkyl, COO-$C_{1-4}$-alkyl;
- piperidinyl, optionally substituted with one or two residues selected from the group consisting of $NHSO_2$-$C_{1-4}$-alkyl, m-methoxyphenyl;
- dihydro-indolyl, dihydro-isoindolyl, tetrahydro-quinolinyl or tetrahydro-isoquinolinyl, optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl, COO-$C_{1-4}$-alkyl, $C_{1-4}$-haloalkyl, O-$C_{1-4}$-alkyl, $NO_2$, halogen;
- a group selected from NHCH(pyridinyl)$CH_2$COO-$C_{1-4}$-alkyl, NHCH($CH_2$O-$C_{1-4}$-alkyl)-benzoimidazolyl, optionally substituted with Cl;
- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazolyl;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl, $C_{1-4}$-haloalkyl, $CH_2CON(C_{1-4}\text{-alkyl})_2$,

$CH_2NHCONH$-$C_{3-6}$-cycloalkyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COO-$C_{1-4}$-alkyl, O-$C_{1-4}$-alkyl, $SO_2$-$C_{1-4}$-alkyl, $SO_2$-$C_{1-4}$-alkylen-OH, $SO_2$-$C_{3-6}$-cycloalkyl, $SO_2$-piperidinyl, $SO_2NH$-$C_{1-4}$-alkyl, $SO_2N(C_{1-4}\text{-alkyl})_2$, halogen, CO-morpholinyl, $CH_2$-pyridinyl, or imidazolidinyl, piperidinyl, oxazinanyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl, pyridinyl, pyrimidinyl, each optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl, $NHC_{1-4}$-alkyl,, =O;

$R^{1.1.1}$ H, $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, $C_{1-4}$-haloalkyl, $CH_2CON(C_{1-4}\text{-alkyl},)_2$, $CH_2CO$-azetindinyl, $C_{1-4}$-alkylen-$C_{3-6}$-cycloalkyl, $CH_2$-pyranyl, $CH_2$-tetrahydrofuranyl, $CH_2$-furanyl, $C_{1-4}$-alkylen-OH or thiadiazolyl, optionally substituted with $C_{1-4}$-alkyl;

$R^{1.1.2}$ H, $C_{1-4}$-alkyl, $SO_2C_{1-4}$-alkyl;

or $R^{1.1.1}$ and $R^{1.1.2}$ together with the nitrogen atom of $CONR^{1.1.1}R^{1.1.2}$ are forming a four-, five- or six-membered heterocyclic ring, optionally containing one O, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of $CH_2OH$

$R^{1.2}$ is selected from

- pyridinyl, pyridazinyl, pyrrolyl, pyrazolyl, isoxazolyl, thiazolyl, thiadiazolyl, optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl, $C_{3-6}$-cycloalkyl, $CH_2COO$-$C_{1-4}$-alkyl, $CONR^{1.2.1}R^{1.2.2}$, COO-$C_{1-4}$-alkyl, $CONH_2$, O-$C_{1-4}$-alkyl, halogen, CO-pyrrolidinyl, CO-morpholinyl or pyrazolyl, triazolyl, tetrazolyl, isoxazolyl, oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl;

- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of $N(C_{1-4}\text{-alkyl})_2$, $CONH\text{-}C_{1-4}\text{-alkyl}$, =O;
- piperidinyl, optionally substituted with pyridinyl;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with $NHCO\text{-}C_{1-4}\text{-alkyl}$,

$R^{1.2.1}$ H, $C_{1-4}$-alkyl;

$R^{1.2.2}$ H, $C_{1-4}$-alkyl;

$R^{1.3}$ is selected from phenyl, pyrazolyl, isoxazolyl, pyrimidinyl, indolyl or oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl, $C_{3-6}$-cycloalkyl, $O\text{-}C_{1-4}$-alkyl, $O\text{-}C_{1-4}$-haloalkyl;

$R^2$ is selected from $CH_2$-phenyl or $CH_2$-naphthyl, both optionally substituted with one or two residues selected from the group consisting of $C_{1-4}$-alkyl, $C_{1-4}$-haloalkyl, $O\text{-}C_{1-4}$-haloalkyl, halogen; or $CH_2$-thiophenyl, optionally substituted with one or two residues selected from the group consisting of halogen;

$R^3$ is H;

$R^4$ is H;

or $R^3$ and $R^4$ together are forming a $CH_2\text{-}CH_2$ group.

4. The use of claim 1 wherein formula 1 is

A is $CH_2$, O or NMe;

$R^1$ is selected from

- $NHR^{1.1}$, $NMeR^{1.1}$;
- $NHR^{1.2}$, $NMeR^{1.2}$;
- $NHCH_2$-$R^{1.3}$;
- NH-piperidinyl, optionally substituted with pyridinyl;
- NH-cyclohexyl, optionally substituted with one or two residues selected from the group consisting of t-Bu, $NHSO_2$-phenyl, NHCONH-phenyl, F;
- NH-pyrrolidinyl, optionally substituted with one or two residues selected from the group consisting of $SO_2Me$, COO-t-Bu;
- piperidinyl, optionally substituted with one or two residues selected from the group consisting of $NHSO_2$-n-Bu, m-methoxyphenyl;
- dihydro-indolyl, dihydro-isoindolyl, tetrahydro-quinolinyl or tetrahydro-isoquinolinyl, optionally substituted with one or two residues selected from the group consisting of Me, COOMe, $CF_3$, OMe, $NO_2$, F, Br;
- a group selected from NHCH(pyridinyl)$CH_2$COOMe, NHCH($CH_2$OMe)-benzoimidazolyl, optionally substituted with Cl;
- or 1-aminocyclopentyl, optionally substituted with methyl-oxadiazolyl;

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, t-Bu, $CF_3$, $CH_2CONMe_2$, $CH_2$NHCONH-cyclohexyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COOMe, COOEt, OMe, $SO_2Me$, $SO_2CH_2CH_2OH$, $SO_2Et$, $SO_2$-cyclopropyl, $SO_2$-piperidinyl, $SO_2NHEt$, $SO_2NMeEt$, F, Cl, CO-morpholinyl, $CH_2$-pyridinyl, or imidazolidinyl, piperidinyl, oxazinanyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl, pyridinyl, pyrimidinyl, each optionally substituted with one or two residues selected from the group consisting of Me, NHMe, =O;

$R^{1.1.1}$ H, Me, Et, t-Bu, i-Pr, cyclopropyl, $CH_2$-i-Pr, $CH_2$-t-Bu, $CH(CH_3)CH_2CH_3$, $CH_2CHF_2$, $CH_2CONMe_2$, $CH_2$CO-azetindinyl, $CH_2$-cyclopropyl, $CH_2$-cyclobutyl, $CH_2$-pyranyl, $CH_2$-tetrahydrofuranyl, $CH_2$-furanyl, $CH_2CH_2OH$ or thiadiazolyl, optionally substituted with Me;

$R^{1.1.2}$ H, Me, Et, $SO_2Me$, $SO_2Et$

or $R^{1.1.1}$ and $R^{1.1.2}$ together with the nitrogen atom of $CONR^{1.1.1}R^{1.1.2}$ are forming a four-, five- or six-membered heterocyclic ring, optionally containing one O, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of $CH_2OH$

$R^{1.2}$ is selected from

- pyridinyl, pyrrolyl, pyrazolyl, isoxazolyl, thiazolyl, thiadiazolyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, Pr, Bu, cyclopropyl, $CH_2COOEt$, $CONR^{1.2.1}R^{1.2.2}$, COOMe, COOEt, $CONH_2$, OMe, Cl, Br CO-pyrrolidinyl, CO-morpholinyl or pyrazolyl, triazolyl, tetrazolyl, isoxazolyl, oxadiazolyl, each optionally substituted Me;
- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of $NMe_2$, CONHMe, =O;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with NHCOMe,

$R^{1.2.1}$ H, Me;

$R^{1.2.2}$ H, Me;

$R^{1.3}$ is selected from phenyl, pyrazolyl, isoxazolyl, pyrimidinyl, indolyl or oxadiazolyl, each optionally substituted with one or two residues selected from the group consisting of Me, Et, Pr, cyclopentyl, OMe, $OCHF_2$;

$R^2$ is selected from $CH_2$-phenyl or $CH_2$-naphthyl, both optionally substituted with one or two residues selected from the group consisting of $CH_3$, $CF_3$, $OCF_3$, F, Cl, Br, Et; or $CH_2$-thiophenyl, optionally substituted with one or two residues selected from the group consisting of Cl, Br;

$R^3$ is H;

$R^4$ is H;

or $R^3$ and $R^4$ together are forming a $CH_2$-$CH_2$ group.

5. The use of claim 1 wherein formula 1 is

A is $CH_2$, O or NMe;

$R^1$ is selected from

- $NHR^{1.1}$
- $NHR^{1.2}$,

$R^{1.1}$ is phenyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, Bu, $CF_3$, $CH_2CONMe_2$, $CH_2NHCONH$-cyclohexyl, CN, $CONR^{1.1.1}R^{1.1.2}$, COOMe, COOEt, OMe, $SO_2Me$, $SO_2CH_2CH_2OH$, $SO_2Et$, $SO_2$-cyclopropyl, $SO_2$-piperidinyl, $SO_2NHEt$, $SO_2NMeEt$, F, Cl, CO-morpholinyl, $CH_2$-pyridinyl, or imidazolidinyl, piperidinyl, oxazinanyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, oxadiazolyl, thiazolyl, pyridinyl, pyrimidinyl, each optionally

substituted with one or two residues selected from the group consisting of Me, NHMe, =O;

$R^{1.1.1}$ H, Me, Et, t-Bu, i-Pr, cyclopropyl, $CH_2$-i-Pr, $CH_2$-t-Bu, $CH(CH_3)CH_2CH_3$, $CH_2CHF_2$, $CH_2CONMe_2$, $CH_2CO$-azetindinyl, $CH_2$-cyclopropyl, $CH_2$-cyclobutyl, $CH_2$-pyranyl, $CH_2$-tetrahydrofuranyl, $CH_2$-furanyl, $CH_2CH_2OH$ or thiadiazolyl, optionally substituted with Me;

$R^{1.1.2}$ H, Me, Et, $SO_2Me$, $SO_2Et$

or $R^{1.1.1}$ and $R^{1.1.2}$ together with the nitrogen atom of $CONR^{1.1.1}R^{1.1.2}$ are forming a four-, five- or six-membered heterocyclic ring, optionally containing one O, replacing a carbon atom of the ring, optionally substituted with one or two residues selected from the group consisting of $CH_2OH$

$R^{1.2}$ is selected from

- pyridinyl, pyrrolyl, pyrazolyl, isoxazolyl, thiazolyl, thiadiazolyl, optionally substituted with one or two residues selected from the group consisting of Me, Et, Pr, Bu, cyclopropyl, $CH_2COOEt$, $CONR^{1.2.1}R^{1.2.2}$, COOMe, COOEt, $CONH_2$, OMe, Cl, Br CO-pyrrolidinyl, CO-morpholinyl or pyrazolyl, triazolyl, tetrazolyl, isoxazolyl, oxadiazolyl, each optionally substituted Me;
- benzothiazolyl, indazolyl, dihydro-indolyl, indanyl, tetrahydro-quinolinyl, each optionally substituted with one or two residues selected from the group consisting of $NMe_2$, CONHMe, =O;
- 4,5-dihydro-naphtho[2,1-d]thiazole, optionally substituted with NHCOMe,

$R^{1.2.1}$ H, Me;

$R^{1.2.2}$ H, Me;

$R^2$ is selected from $CH_2$-phenyl or $CH_2$-naphthyl, both optionally substituted with one or two residues selected from the group consisting of $CH_3$, $CF_3$, $OCF_3$, F, Cl, Br, Et

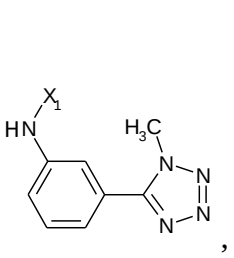
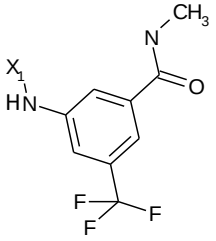
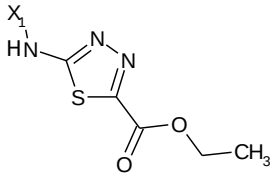
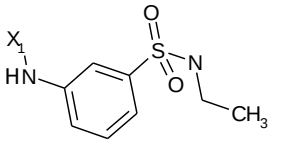
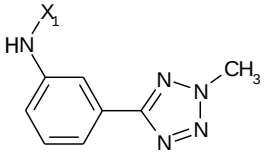
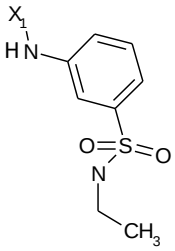
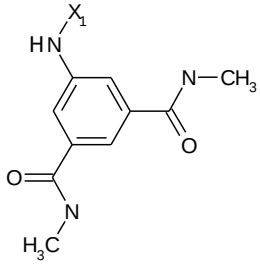
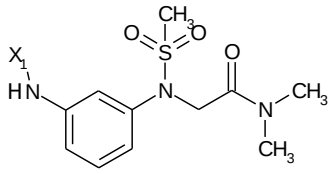
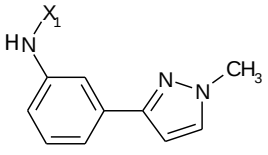
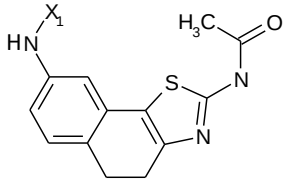
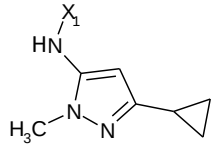
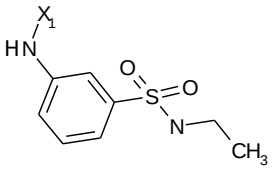
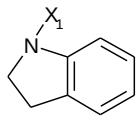
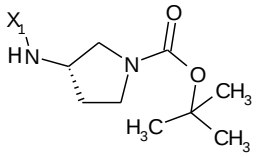
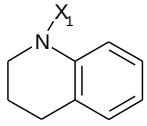
$R^3$ is H;

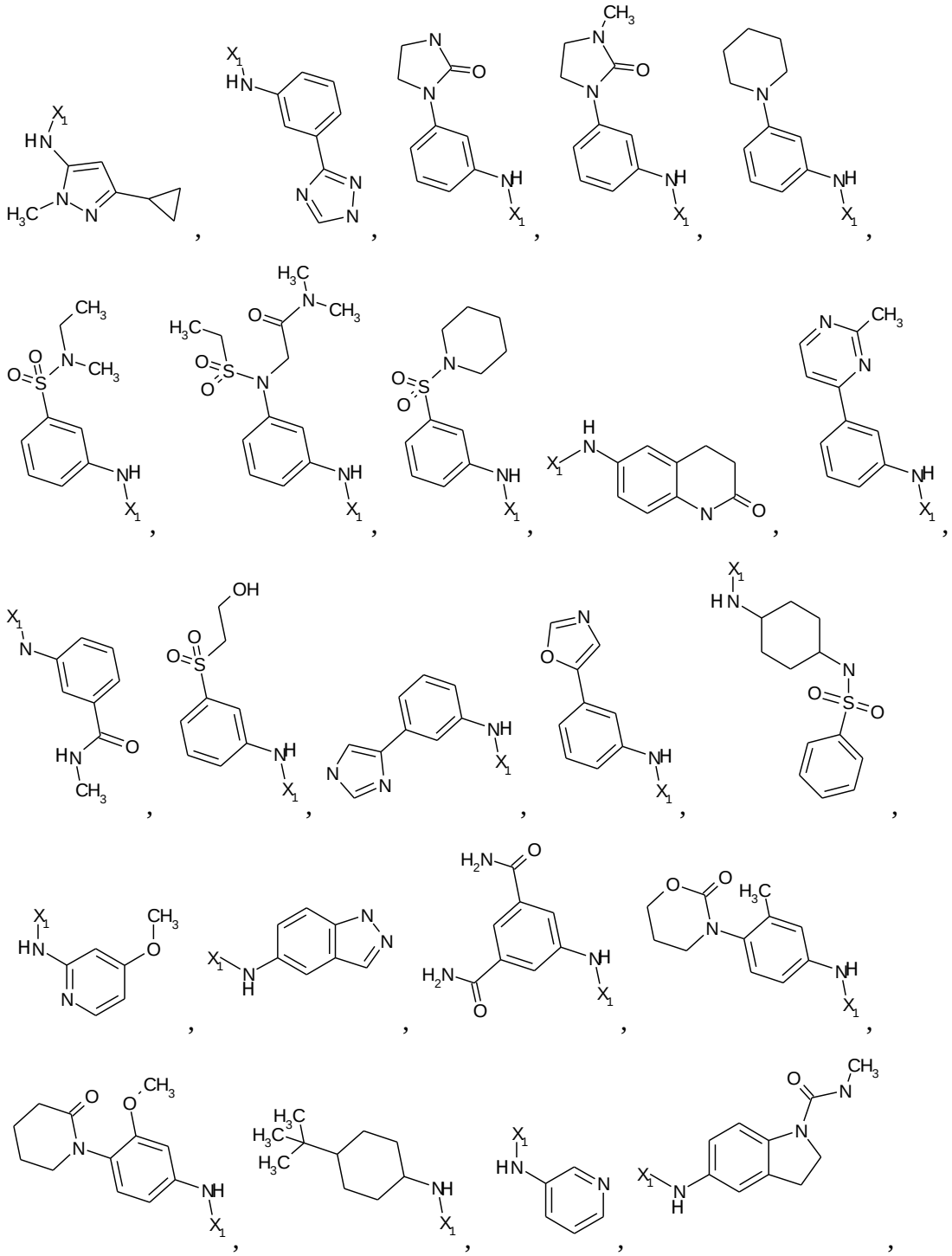
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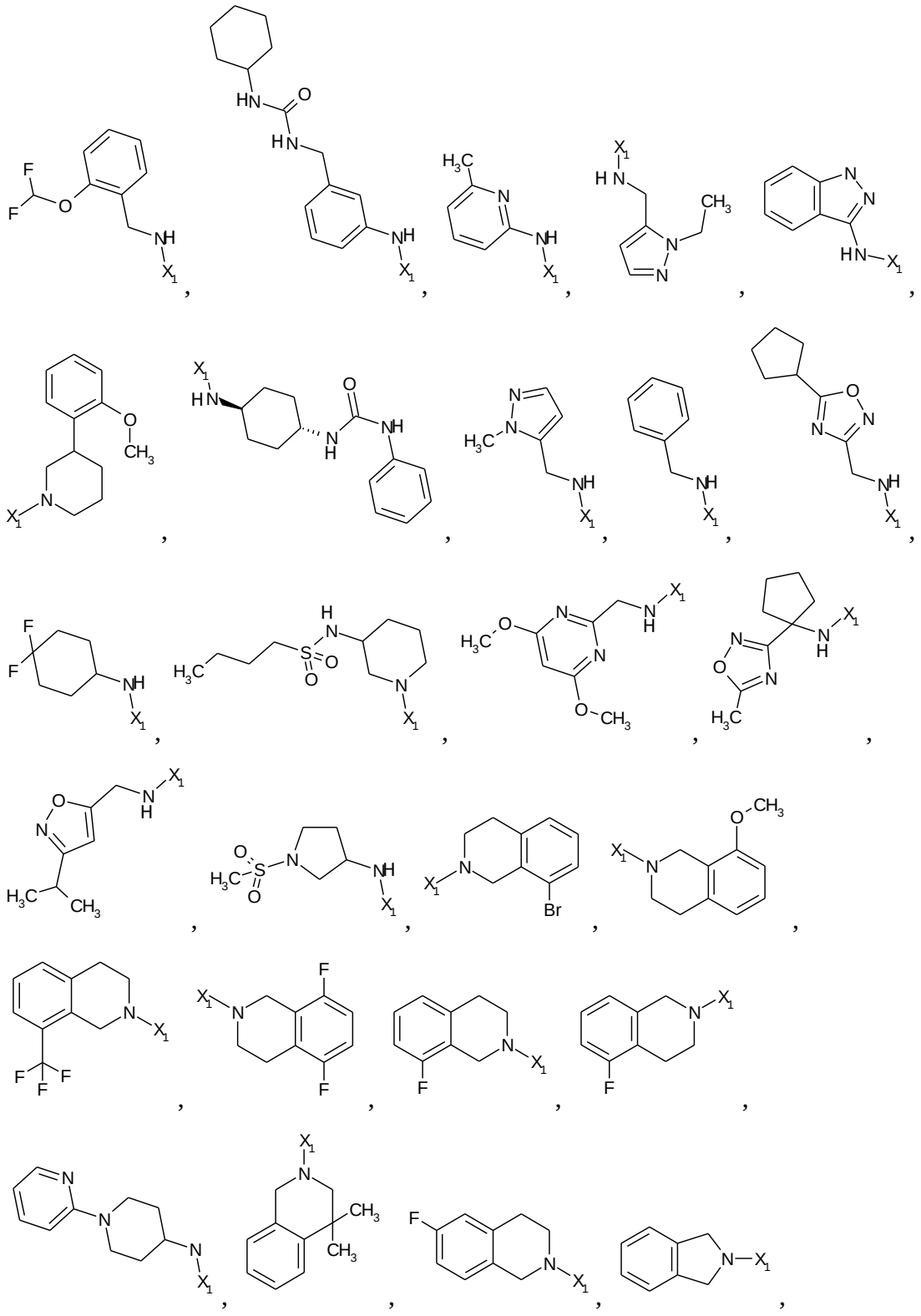
6. The use of claim 1 wherein formula 1 is

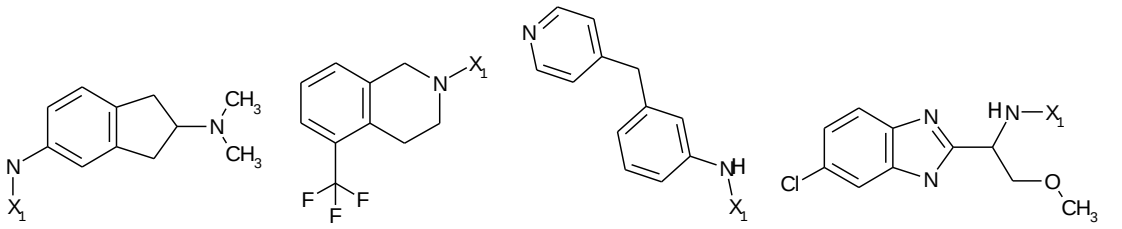
A is $CH_2$, O or NMe;

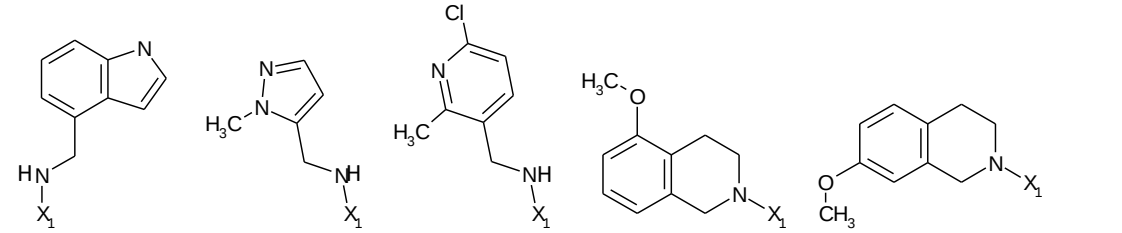
$R^1$ is selected from

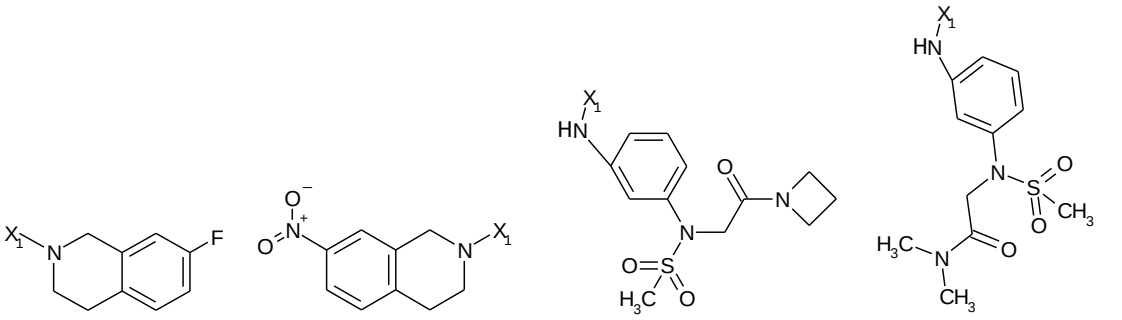

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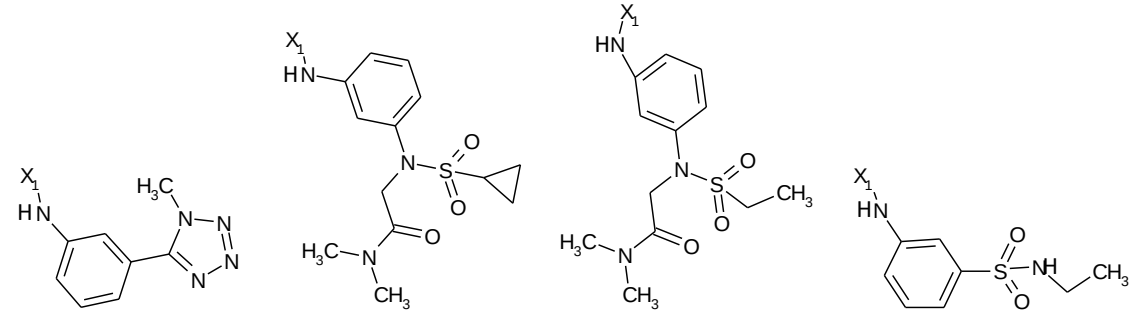


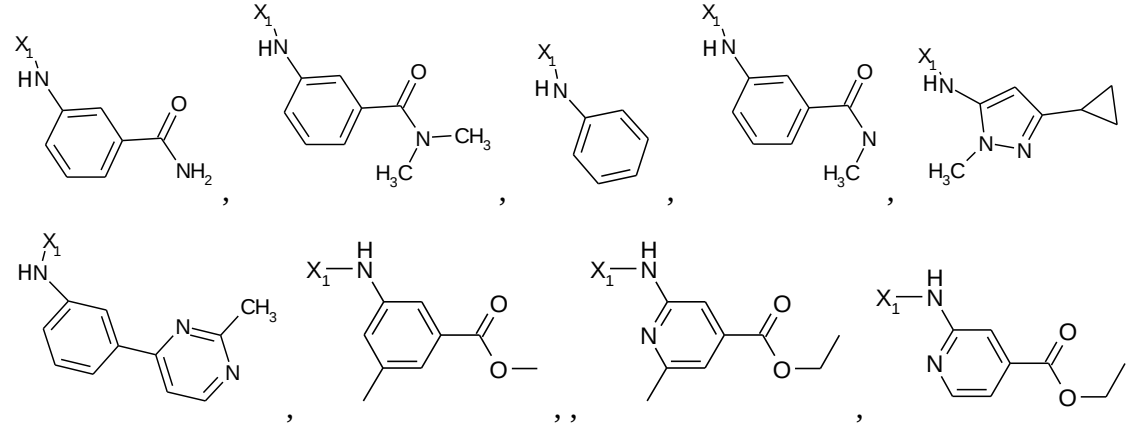


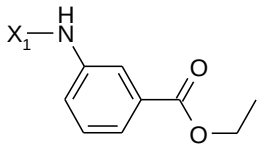
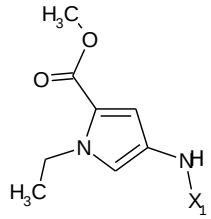
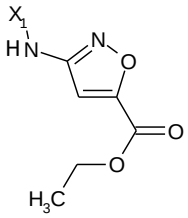
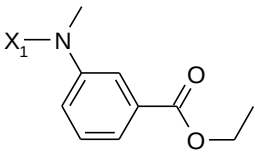
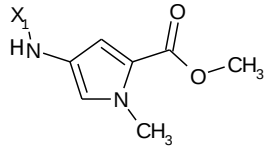
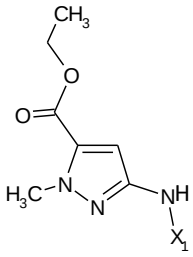
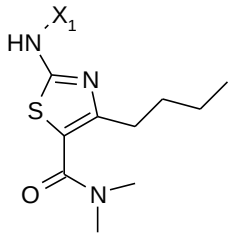
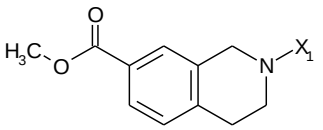
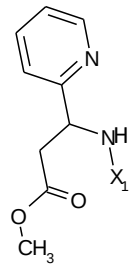
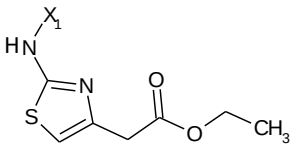
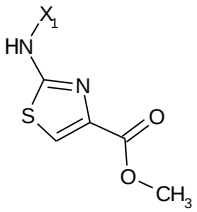
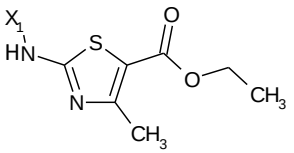
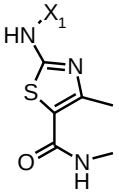
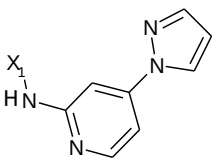
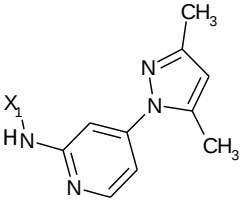
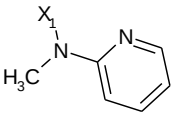
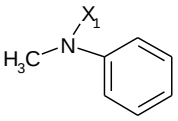
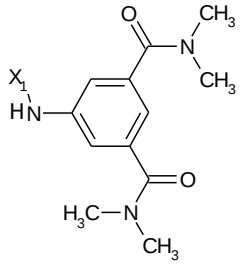
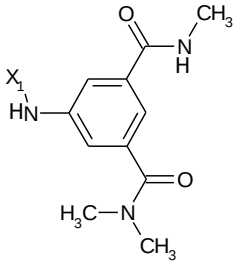
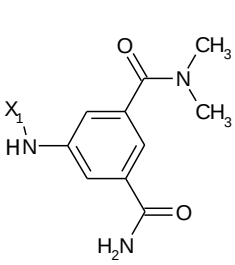
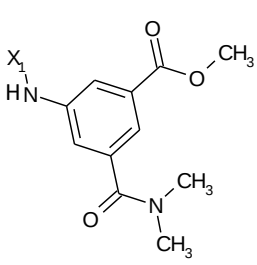


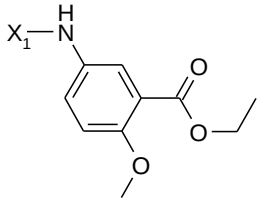
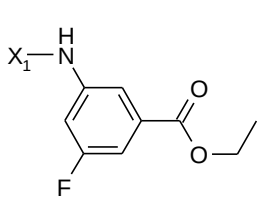
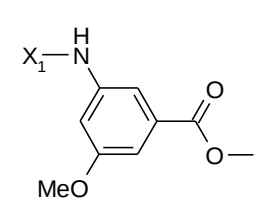
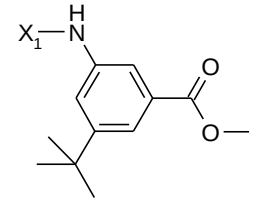









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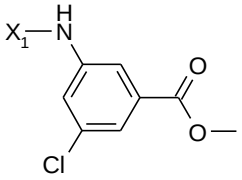
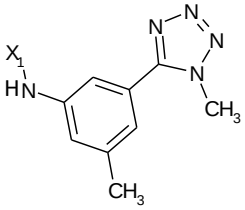
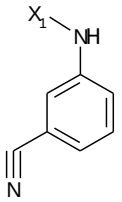
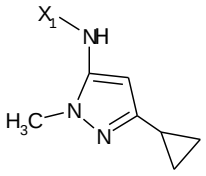
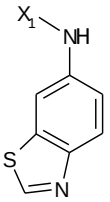
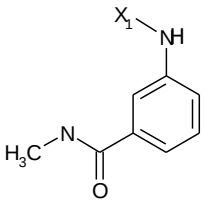
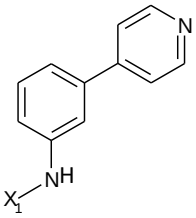
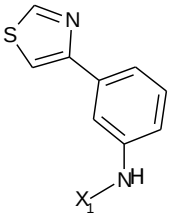
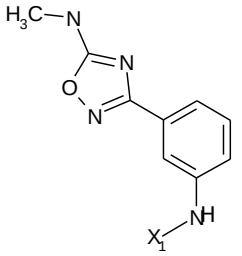
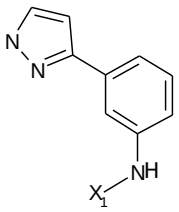
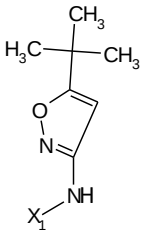
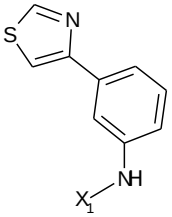
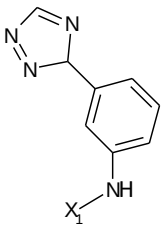
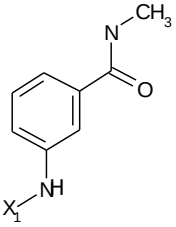
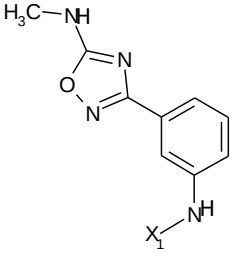
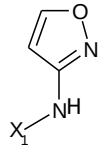
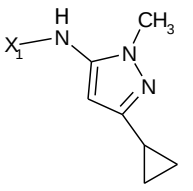
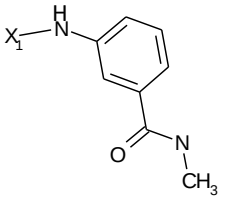
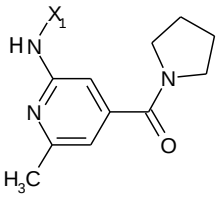
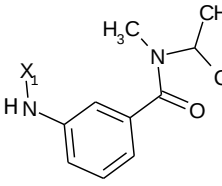
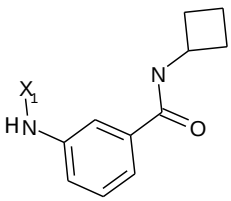
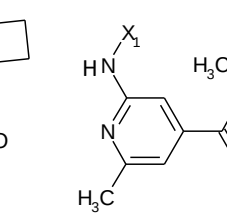
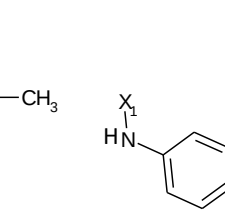
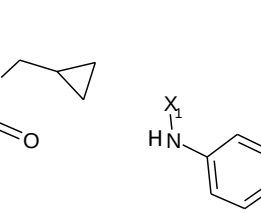
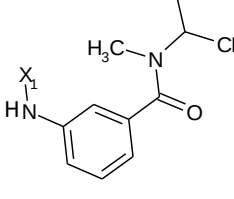
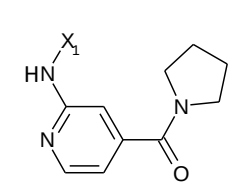
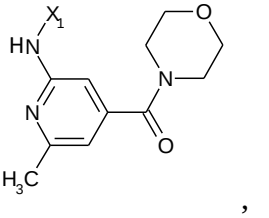
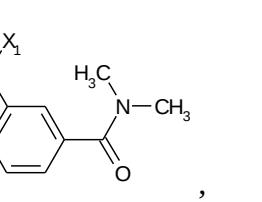
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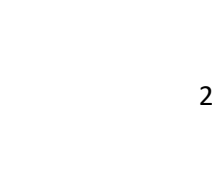
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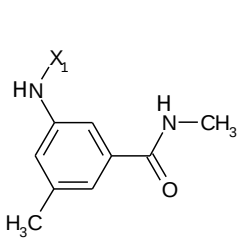
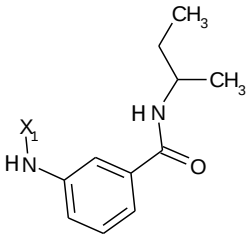
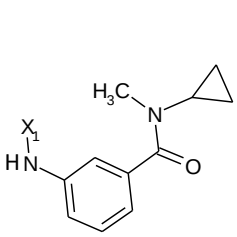
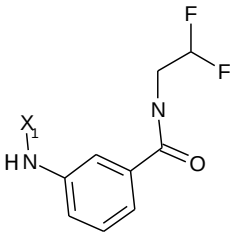
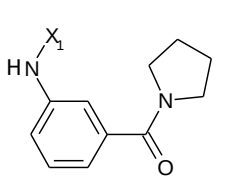
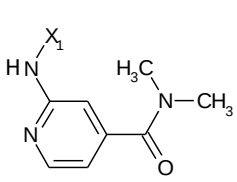
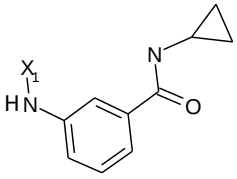
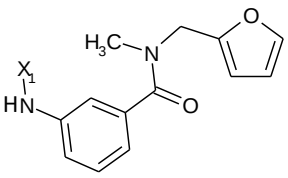
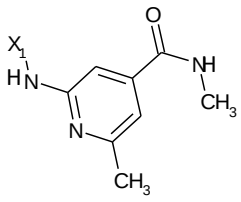
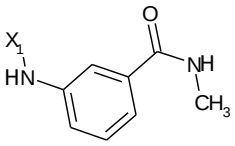
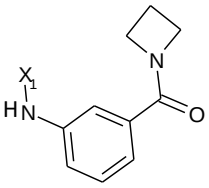
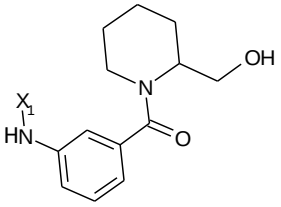
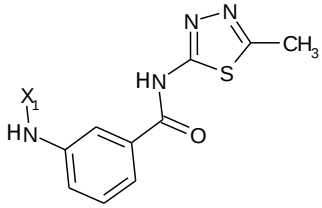
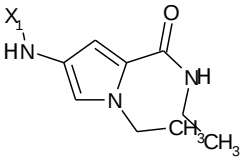
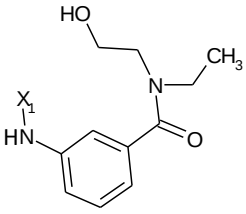
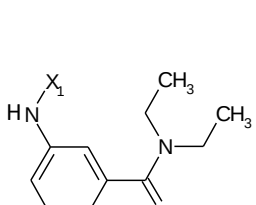
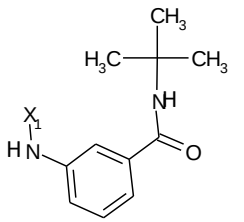
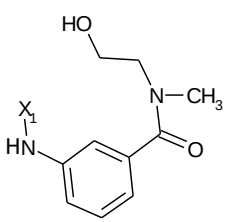
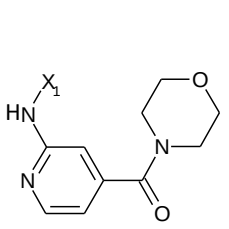
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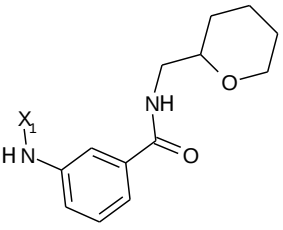
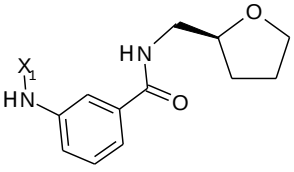
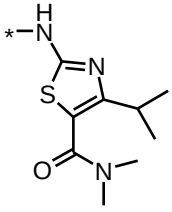
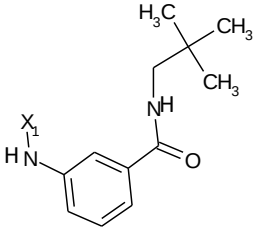
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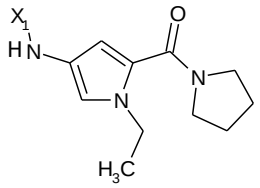
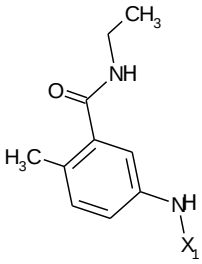
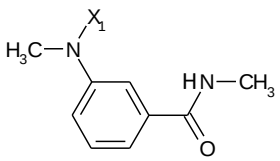
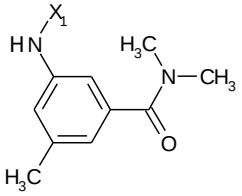
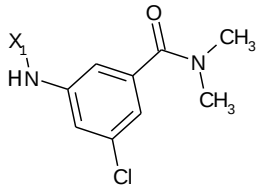
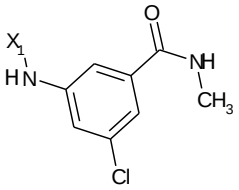
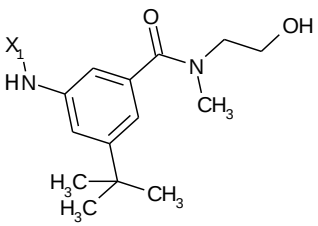
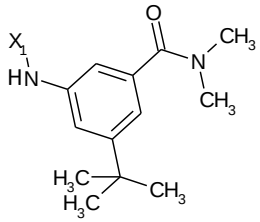
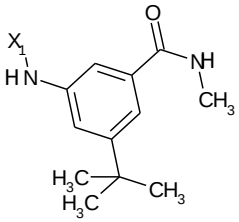
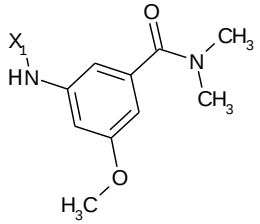
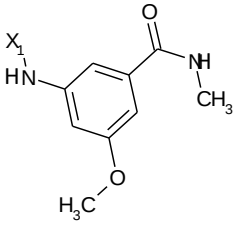
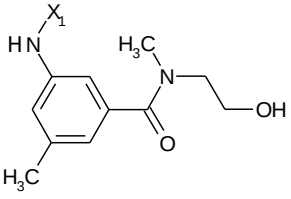
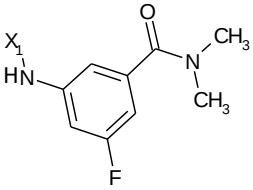
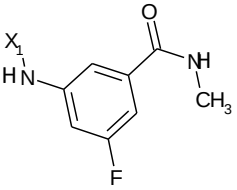
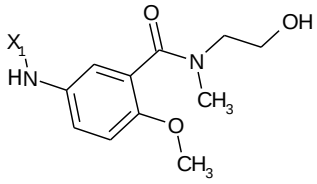
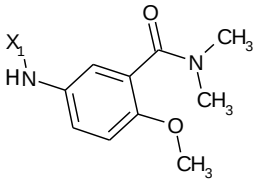
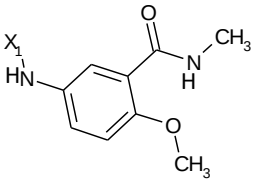
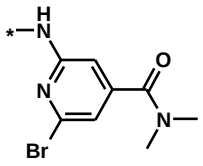
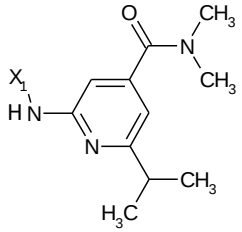
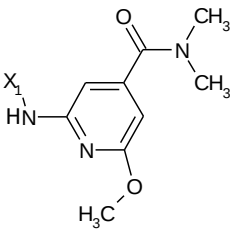
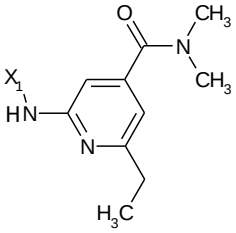
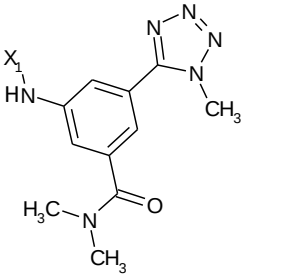
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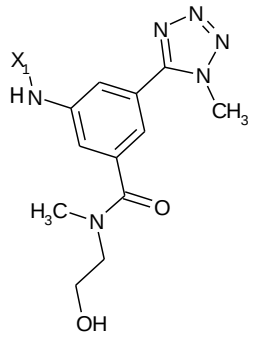
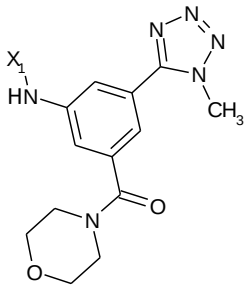
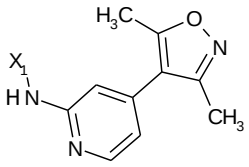
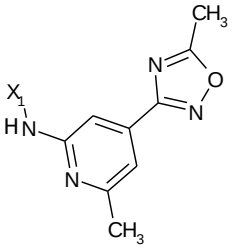
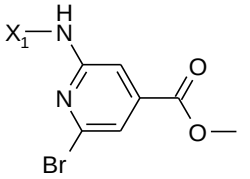
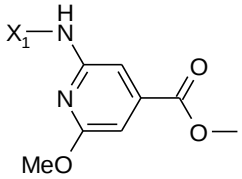
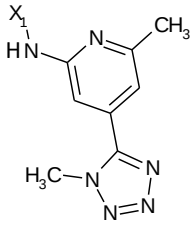
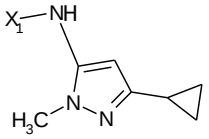
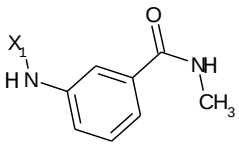
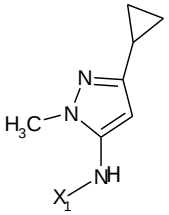
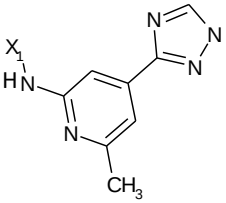
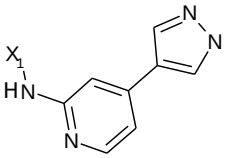
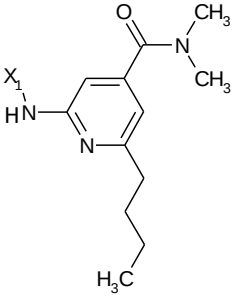
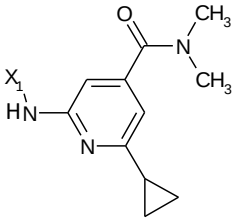
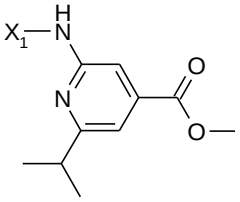
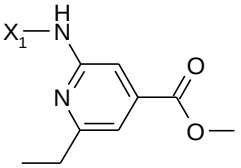

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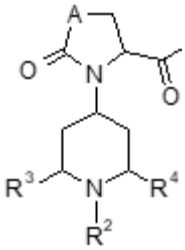
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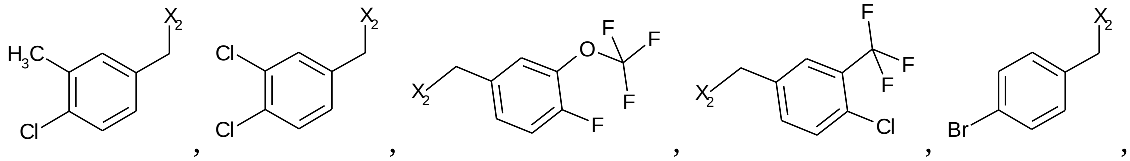

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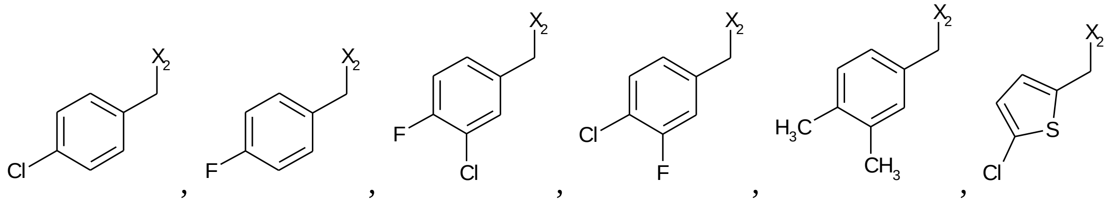

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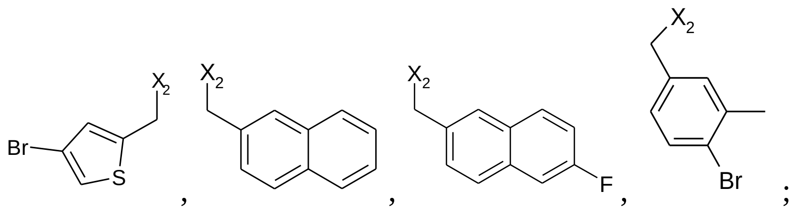
wherein $X_1$ is:


, wherein $R^1$ is attached to the vacant single bond;

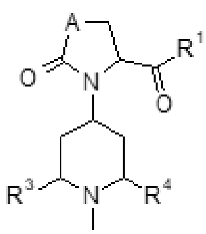
$R^2$ is selected from







wherein $X_2$ is:



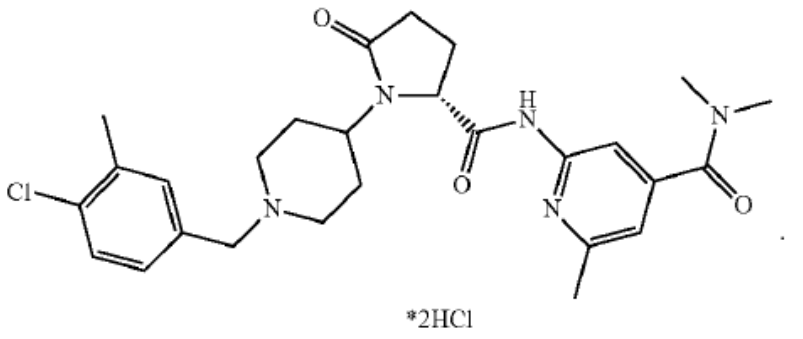
, wherein $R^2$ is attached to the vacant single bond;

$R^3$ is H;

$R^4$ is H;

or $R^3$ and $R^4$ together are forming a $CH_2$-$CH_2$ group.

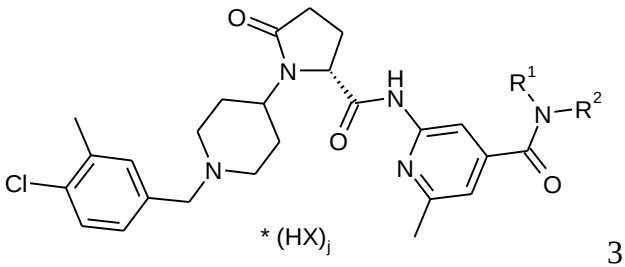
7. Use of a crystalline salt of a compound of the formula below in the manufacture of a medicament for treating aging-associated neuronal loss, memory impairment, or loss of motor coordination in a subject diagnosed with the aging-associated neuronal loss, memory impairment, or loss of motor coordination, wherein the medicament is to be administered in the subject




8. Use of a pharmaceutical composition comprising at least one co-crystal of the crystalline salt of the compound of claim 7 and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating aging-associated neuronal loss, memory impairment, or loss of motor coordination in a subject, wherein the pharmaceutical composition is to be administered in the subject.

9. The use of claim 1 wherein the compound of formula 1 is to be administered in the form of the individual optical isomers, a mixture of the individual enantiomers, a racemate or in the form of the enantiomerically pure compounds.

10. Use of a pharmaceutical composition comprising a compound of formula 3 in the manufacture of a medicament for treating aging-associated neuronal loss, memory impairment, or loss of motor coordination in a subject, wherein the compound of formula 3 is to be administered in the subject and has the following formula:




3

wherein

$R^1$ is H, $C_{1-6}$-alkyl, $C_{0-4}$-alkyl-$C_{3-6}$-cycloalkyl, $C_{1-6}$-haloalkyl;

$R^2$ is H, $C_{1-6}$-alkyl;

X is an anion selected from the group consisting of chloride or ½ dibenzoyltartrate

j is 1 or 2,

and the pharmaceutical composition further comprises a first diluent, a second diluent, a binder, a disintegrant and a lubricant.

11. The use of claim 10 wherein the pharmaceutical composition further comprises an additional disintegrant.

12. The use of claim 10 or 11 wherein the pharmaceutical composition further comprises a glidant.

13. The use of claim 10, 11 or 12 wherein the diluent of the pharmaceutical composition further comprises cellulose powder, dibasic calciumphosphate anhydrous, dibasic calciumphosphate dehydrate, erythritol, low substituted hydroxypropyl cellulose, mannitol, pregelatinized starch, or xylitol.

14. The use of claim 1, wherein the medicament is for treating aging-associated neuronal loss.

15. The use of claim 1, wherein the medicament is for treating aging-associated memory impairment.

16. The use of claim 1, wherein the medicament is for treating aging-associated motor coordination.

17. The use of any of the preceding claims, wherein the compound or the pharmaceutical composition comprising the compound is to be administered orally or via inhalation in the subject.

18. The use of the pharmaceutical composition of claim 8, wherein the co-crystal former is selected from the group consisting of orotic acid, hippuric acid, L-pyroglutamic acid, D-pyroglutamic acid, nicotinic acid, L-(+)-ascorbic acid, saccharin, piperazine, 3-hydroxy-2-naphtoic acid, mucic (galactaric) acid, pamoic (embonic) acid, stearic acid, cholic acid, deoxycholic acid, nicotinamide, isonicotinamide, succinamide, uracil, L-lysine, L-proline, D-valine, L-arginine, and glycine.