

(I)

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein

X^1 is $N(R^{a1})$;

X^{1a} is ~~a covalent single bond,~~ $CH(R^{a3})$~~, or $CH(R^{a3})CH_2$~~;

R^{a1} is H, $C(O)OC_{1-4}$ alkyl, or C_{1-4} alkyl, wherein $C(O)OC_{1-4}$ alkyl and C_{1-4} alkyl are optionally substituted with one or more substituents selected from the group consisting of halogen, OH, and O-C_{1-3} alkyl, wherein the substituents are the same or different;

R^{a2}, R^{a3} are independently selected from the group consisting of H, OH, OC_{1-4} alkyl, halogen, C_{1-4} alkyl, and A^{2a}; and

R^{a4}, R^{a5}, R^{a6}, R^{a7} are independently selected from the group consisting of H, halogen, C_{1-4} alkyl, and A^{2a},

provided that only one of R^{a2}, R^{a3}, R^{a4}, R^{a5}, R^{a6}, R^{a7} is A^{2a};

or R^{a1} and one of R^{a2} and R^{a3} form a methylene or ethylene group;

or R^{a1} and R^{a6} form an ethylene group;

or R^{a2} and R^{a5} form a covalent single bond;

or R^{a5}, R^{a7} are joined to form an oxo group;

A^1 is C_5 cycloalkylene, C_5 cycloalkenylene, or a nitrogen ring atom containing 5-membered heterocyclene, wherein A^1 is optionally substituted with one or more R^4, which are the same or different;

each R^4 is independently oxo (=O) where the ring is at least partially saturated, thiooxo (=S) where the ring is at least partially saturated, halogen, CN, OR^5, or C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

R^5 is H or C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

A^2 is R^{6a} or A^{2a};

~~R^{6a} is OR^{6a1}, SR^{6a1}, $N(R^{6a1}R^{6a2})$; C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more substituents selected from the group consisting of halogen; OR^{6a3}; CN; and A^{2a}, wherein the substituents are the same or different;~~

~~R^{6a1}, R^{6a2} are independently selected from the group consisting of H; C_{1-6} alkyl; C_{2-6} alkenyl; C_{2-6} alkynyl; and A^{2a}, wherein C_{1-6} alkyl; C_{2-6} alkenyl; and C_{2-6} alkynyl are optionally substituted with one or more substituents selected from the group consisting of halogen; CN; OR^{6a3}; OA^{2a} and A^{2a}, wherein the substituents are the same or different;~~

R^{6a} is OR^{6a1} and R^{6a1} is A^{2a} or C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3}; or R^{6a} is C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3};

R^{6a3} is H, or C_{1-4} alkyl, wherein C_{1-4} alkyl is optionally substituted with one or more halogen, which are the same or different;

A^{2a} is phenyl, C_{3-7} cycloalkyl, C_{4-12} bicycloalkyl, or 3- to 7-membered heterocyclyl, wherein A^{2a} is optionally substituted with one or more R^6, which are the same or different;

each R^6 is independently R^{6b}, OH; OR^{6b}, halogen; or CN, wherein R^{6b} is cyclopropyl, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein R^{6b} is optionally substituted with one or more halogen, which are the same or different; or
two R^6 are joined to form together with the atoms to which they are attached a ring A^{2b};

A^{2b} is phenyl, C_{3-7} cycloalkyl, or 3 to 7 membered heterocyclyl, wherein A^{2b} is optionally substituted with one or more R^7, which are the same or different;

each R^7 is independently C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different;

R^1 is H or C_{1-4} alkyl, preferably H, wherein C_{1-4} alkyl is optionally substituted with one or more halogen, which are the same or different;

R^2 is H, F, or C_{1-4} alkyl, wherein C_{1-4} alkyl is optionally substituted with one or more halogen, which are the same or different; and

R^3 is A^3, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more R^8, which are the same or different; or

R^2 and R^3 are joined to form together with the oxygen atom and carbon atom to which they are attached a ring A^{3a}, wherein A^{3a} is a 7 to 12 membered heterobicyclyl, wherein 7 to 12 membered heterobicyclyl is optionally substituted with one or more R^{10}, which are the same or different;

R^{2a} is H or F, preferably H;

each R^8 is independently halogen, CN, $C(O)OR^9$, OR^9, $C(O)R^9$, $C(O)N(R^9R^{9a})$, $S(O)_2N(R^9R^{9a})$, $S(O)N(R^9R^{9a})$, $S(O)_2R^9$, $S(O)R^9$, $N(R^9)S(O)_2N(R^{9a}R^{9b})$, SR^9, $N(R^9R^{9a})$, NO_2, $OC(O)R^9$, $N(R^9)C(O)R^{9a}$, $N(R^9)SO_2R^{9a}$, $N(R^9)S(O)R^{9a}$, $N(R^9)C(O)N(R^{9a}R^{9b})$, $N(R^9)C(O)OR^{9a}$, $OC(O)N(R^9R^{9a})$, or A^3;

R^9, R^{9a}, R^{9b} are independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different, or one OH, or one OC_{1-4} alkyl, or one A^3;

each A^3 is independently phenyl, naphthyl, C_{3-7} cycloalkyl, 3 to 7 membered heterocyclyl, or 7 to 12 membered heterobicyclyl, wherein A^3 is optionally substituted with one or more R^{10}, which are the same or different;

each R^{10} is independently halogen, CN, $C(O)OR^{11}$, OR^{11}, $C(O)R^{11}$, $C(O)N(R^{11}R^{11a})$, $S(O)_2N(R^{11}R^{11a})$, $S(O)N(R^{11}R^{11a})$, $S(O)_2R^{11}$, $S(O)R^{11}$, $N(R^{11})S(O)_2N(R^{11a}R^{11b})$, SR^{11},

$N(R^{11}R^{11a})$, NO_2, $OC(O)R^{11}$, $N(R^{11})C(O)R^{11a}$, $N(R^{11})S(O)_2R^{11a}$, $N(R^{11})S(O)R^{11a}$, $N(R^{11})C(O)OR^{11a}$, $N(R^{11})C(O)N(R^{11a}R^{11b})$, $OC(O)N(R^{11}R^{11a})$, oxo (=O) where the ring is at least partially saturated, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more R^{12}, which are the same or different;

R^{11}, R^{11a}, R^{11b} are independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different;

each R^{12} is independently halogen, CN, $C(O)OR^{13}$, OR^{13}, $C(O)R^{13}$, $C(O)N(R^{13}R^{13a})$, $S(O)_2N(R^{13}R^{13a})$, $S(O)N(R^{13}R^{13a})$, $S(O)_2R^{13}$, $S(O)R^{13}$, $N(R^{13})S(O)_2N(R^{13a}R^{13b})$, SR^{13}, $N(R^{13}R^{13a})$, NO_2, $OC(O)R^{13}$, $N(R^{13})C(O)R^{13a}$, $N(R^{13})SO_2R^{13a}$, $N(R^{13})S(O)R^{13a}$, $N(R^{13})C(O)N(R^{13a}R^{13b})$, $N(R^{13})C(O)OR^{13a}$, or $OC(O)N(R^{13}R^{13a})$;

R^{13}, R^{13a}, R^{13b} are independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different.

~~In another aspect, the present disclosure refers to a compound as defined above or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof for the use as a medicament.~~

In yet another aspect, the present disclosure refers to a pharmaceutical composition comprising at least one compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined above together with a pharmaceutically acceptable carrier, optionally in combination with one or more other bioactive compounds or pharmaceutical compositions.

~~In yet another aspect, the present disclosure refers to a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined above or a pharmaceutical composition as defined above for use in treating or preventing of one or more diseases or disorders associated with integrated stress response.~~

~~In yet another aspect, the present disclosure refers to a use of a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined above or a pharmaceutical composition as defined above in the manufacture of a medicament for the treatment or prevention of one or more diseases or disorders associated with integrated stress response.~~

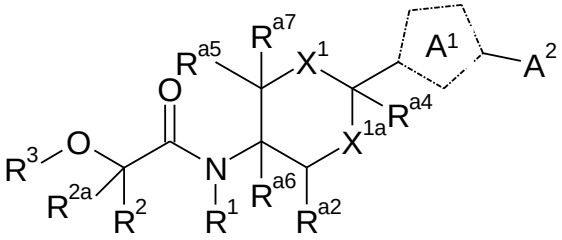
In yet another aspect, the present disclosure refers to a use of a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined above or a pharmaceutical composition as defined above in the manufacture of a medicament for treating or preventing of one or more diseases or disorders selected from the group consisting of leukodystrophies, intellectual disability syndrome, neurodegenerative diseases and disorders, neoplastic diseases, infectious diseases, inflammatory diseases, musculoskeletal diseases, metabolic diseases, ocular diseases as well as diseases selected from the group consisting of organ fibrosis, chronic and acute diseases of the liver, chronic and acute diseases of the lung, chronic and acute diseases of the kidney, myocardial infarction, cardiovascular disease, arrhythmias, atherosclerosis, spinal cord injury, ischemic stroke, and neuropathic pain.

In another aspect, there is provide a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined above or a pharmaceutical composition as defined above for use as a medicament

A compound not restricted to the use as a medicament as defined above with preferences as defined below and a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, is also within the scope of the present disclosure provided that the following compounds or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof are excluded:

Patent Claims

1. A compound of formula (I)



(I)

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein

X^1 is $N(R^{a1})$;

X^{1a} is ~~a covalent single bond,~~ $CH(R^{a3})$~~, or $CH(R^{a3})CH_2$~~;

R^{a1} is H, $C(O)OC_{1-4}$ alkyl, or C_{1-4} alkyl, wherein $C(O)OC_{1-4}$ alkyl and C_{1-4} alkyl are optionally substituted with one or more substituents selected from the group consisting of halogen, OH, and $O\text{-}C_{1-3}$ alkyl, wherein the substituents are the same or different;

R^{a2}, R^{a3} are independently selected from the group consisting of H, OH, OC_{1-4} alkyl, halogen, C_{1-4} alkyl, and A^{2a}; and

R^{a4}, R^{a5}, R^{a6}, R^{a7} are independently selected from the group consisting of H, halogen, C_{1-4} alkyl, and A^{2a},

provided that only one of R^{a2}, R^{a3}, R^{a4}, R^{a5}, R^{a6}, R^{a7} is A^{2a};

or R^{a1} and one of R^{a2} and R^{a3} form a methylene or ethylene group;

or R^{a1} and R^{a6} form an ethylene group;

or R^{a2} and R^{a5} form a covalent single bond;

or R^{a5}, R^{a7} are joined to form an oxo group;

A^1 is C_5 cycloalkylene, C_5 cycloalkenylene, or a nitrogen ring atom containing 5-membered heterocyclene, wherein A^1 is optionally substituted with one or more R^4, which are the same or different;

each R^4 is independently oxo (=O) where the ring is at least partially saturated, thiooxo (=S) where the ring is at least partially saturated, halogen, CN, OR^5, or C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

R^5 is H or C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

A^2 is R^{6a} or A^{2a};

~~R^{6a} is OR^{6a1}, SR^{6a1}, $N(R^{6a1}R^{6a2})$; C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more substituents selected from the group consisting of halogen; OR^{6a3}; CN; and A^{2a}; wherein the substituents are the same or different;~~

~~R^{6a1}, R^{6a2} are independently selected from the group consisting of H; C_{1-6} alkyl; C_{2-6} alkenyl; C_{2-6} alkynyl; and A^{2a}, wherein C_{1-6} alkyl; C_{2-6} alkenyl; and C_{2-6} alkynyl are optionally substituted with one or more substituents selected from the group consisting of halogen; CN; OR^{6a3}; OA^{2a} and A^{2a}, wherein the substituents are the same or different;~~

R^{6a} is OR^{6a1} and R^{6a1} is A^{2a} or C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3}; or R^{6a} is C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3};

R^{6a3} is H~~;~~, or C_{1-4} alkyl, wherein C_{1-4} alkyl is optionally substituted with one or more halogen, which are the same or different;

A^{2a} is phenyl~~;~~, C_{3-7} cycloalkyl~~;~~, C_{4-12} bicycloalkyl~~;~~, or 3- to 7-membered heterocyclyl, wherein A^{2a} is optionally substituted with one or more R^6, which are the same or different;

each R^6 is independently R^{6b}, OH, OR^{6b}, halogen, or CN, wherein R^{6b} is cyclopropyl, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein R^{6b} is optionally substituted with one or more halogen, which are the same or different; or
two R^6 are joined to form together with the atoms to which they are attached a ring A^{2b};

A^{2b} is phenyl, C_{3-7} cycloalkyl, or 3 to 7 membered heterocyclyl, wherein A^{2b} is optionally substituted with one or more R^7, which are the same or different;

each R^7 is independently C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different;

R^1 is H or C_{1-4} alkyl, preferably H, wherein C_{1-4} alkyl is optionally substituted with one or more halogen, which are the same or different;

R^2 is H, F, or C_{1-4} alkyl, wherein C_{1-4} alkyl is optionally substituted with one or more halogen, which are the same or different; and
R^3 is A^3, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more R^8, which are the same or different; or
R^2 and R^3 are joined to form together with the oxygen atom and carbon atom to which they are attached a ring A^{3a}, wherein A^{3a} is a 7 to 12 membered heterobicyclyl, wherein 7 to 12 membered heterobicyclyl is optionally substituted with one or more R^{10}, which are the same or different;

R^{2a} is H or F, preferably H;

each R^8 is independently halogen, CN, $C(O)OR^9$, OR^9, $C(O)R^9$, $C(O)N(R^9R^{9a})$, $S(O)_2N(R^9R^{9a})$, $S(O)N(R^9R^{9a})$, $S(O)_2R^9$, $S(O)R^9$, $N(R^9)S(O)_2N(R^{9a}R^{9b})$, SR^9, $N(R^9R^{9a})$, NO_2, $OC(O)R^9$, $N(R^9)C(O)R^{9a}$, $N(R^9)SO_2R^{9a}$, $N(R^9)S(O)R^{9a}$, $N(R^9)C(O)N(R^{9a}R^{9b})$, $N(R^9)C(O)OR^{9a}$, $OC(O)N(R^9R^{9a})$, or A^3;

R^9, R^{9a}, R^{9b} are independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different, or one OH, or one OC_{1-4} alkyl, or one A^3;

each A^3 is independently phenyl, naphthyl, C_{3-7} cycloalkyl, 3 to 7 membered heterocyclyl, or 7 to 12 membered heterobicyclyl, wherein A^3 is optionally substituted with one or more R^{10}, which are the same or different;

each R^{10} is independently halogen, CN, $C(O)OR^{11}$, OR^{11}, $C(O)R^{11}$, $C(O)N(R^{11}R^{11a})$, $S(O)_2N(R^{11}R^{11a})$, $S(O)N(R^{11}R^{11a})$, $S(O)_2R^{11}$, $S(O)R^{11}$, $N(R^{11})S(O)_2N(R^{11a}R^{11b})$, SR^{11}, $N(R^{11}R^{11a})$, NO_2, $OC(O)R^{11}$, $N(R^{11})C(O)R^{11a}$, $N(R^{11})S(O)_2R^{11a}$, $N(R^{11})S(O)R^{11a}$, $N(R^{11})C(O)OR^{11a}$, $N(R^{11})C(O)N(R^{11a}R^{11b})$, $OC(O)N(R^{11}R^{11a})$, oxo (=O) where the ring is at least partially saturated, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more R^{12}, which are the same or different;

R^{11}, R^{11a}, R^{11b} are independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different;

each R^{12} is independently halogen, CN, $C(O)OR^{13}$, OR^{13}, $C(O)R^{13}$, $C(O)N(R^{13}R^{13a})$, $S(O)_2N(R^{13}R^{13a})$, $S(O)N(R^{13}R^{13a})$, $S(O)_2R^{13}$, $S(O)R^{13}$, $N(R^{13})S(O)_2N(R^{13a}R^{13b})$, SR^{13}, $N(R^{13}R^{13a})$, NO_2, $OC(O)R^{13}$, $N(R^{13})C(O)R^{13a}$, $N(R^{13})SO_2R^{13a}$, $N(R^{13})S(O)R^{13a}$, $N(R^{13})C(O)N(R^{13a}R^{13b})$, $N(R^{13})C(O)OR^{13a}$, or $OC(O)N(R^{13}R^{13a})$;

R^{13}, R^{13a}, R^{13b} are independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different.

2. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein X^1 is NH or N-C_{1-4} alkyl, wherein C_{1-4} alkyl is optionally substituted with one or more substituents selected from the group consisting of halogen, OH, and O-C_{1-3} alkyl, wherein the substituents are the same or

different; preferably NH, $N(CH_3)$, $N(CH_2CH_3)$, or $N(CH_2CH_2OCH_3)$; more preferably, NH or $N(CH_3)$; even more preferably NH.

~~3. The compound of claim 1 or 2 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein X^{1a} is $CH(R^{a3})$ or $CH(R^{a3})CH_2$, preferably $CH(R^{a3})$.~~

43. The compound of ~~any one of~~ claim~~s~~ 1 ~~to~~or 2~~3~~ or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein

R^{a2}, R^{a3} are independently selected from the group consisting of H~~;~~, OH~~;~~, OC_{1-4} alkyl~~;~~, halogen~~;~~, C_{1-4} alkyl~~;~~ and A^{2a}; and

R^{a4}, R^{a5}, R^{a6}, R^{a7} are independently selected from the group consisting of H~~;~~, halogen~~;~~, C_{1-4} alkyl~~;~~ and A^{2a}, provided that only one of R^{a2}, R^{a3}, R^{a4}, R^{a5}, R^{a6}, R^{a7} is A^{2a};

or R^{a5}, R^{a7} are joined to form an oxo group;

preferably wherein R^{a2}, R^{a3}, R^{a4}, R^{a5}, R^{a6}, R^{a7} are H or wherein R^{a2}, R^{a3}, R^{a4}, R^{a6} are H and R^{a5}, R^{a7} are joined to form an oxo group.

54. The compound of any one of claims 1 to 3~~4~~ or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{a2}, R^{a3}, R^{a4}, R^{a5}, R^{a6}, R^{a7} are H.

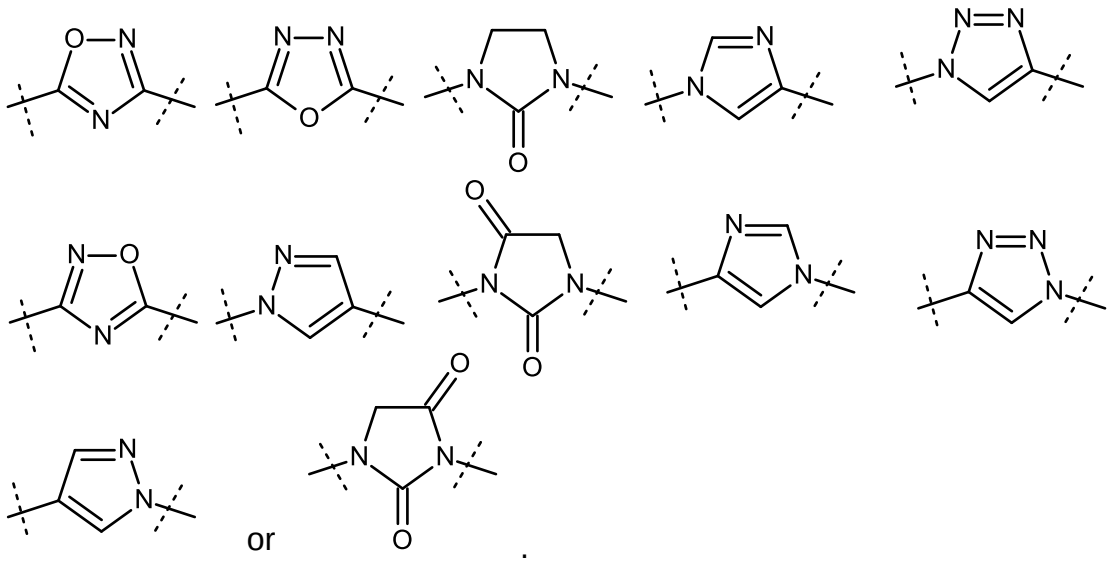
65. The compound of any one of claims 1 to ~~5~~4 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^1 is a nitrogen ring atom containing 5-membered heterocyclene and wherein A^1 is optionally substituted with one or more R^4, which are the same or different.

~~7~~6. The compound of any one of claims 1 to ~~6~~5 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^1 is a nitrogen ring atom containing 5-membered heterocyclene selected from the group of bivalent heterocycles consisting of oxadiazole, imidazole, imidazolidine, pyrazole and triazole, preferably oxadiazole, and wherein A^1 is optionally substituted with one or more R^4, which are the same or different.

~~8~~7. The compound of any one of claims 1 to ~~6~~7 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^1 is unsubstituted or substituted with one or two R^4, which are the same or different, preferably A^1 is unsubstituted.

~~9~~8. The compound of any one of claims 1 to ~~7~~8 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^4 is oxo, where the ring is at least partly saturated.

~~10~~9. The compound of any one of claims 1 to ~~9~~8 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^1 is



~~11~~10. The compound of any one of claims 1 to ~~9~~10 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^2 is R^{6a}.

~~12. The compound of claim 11 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{6a} is OR^{6a1} and R^{6a1} is preferably A^{2a} or C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3}; or R^{6a} is C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3}.~~

~~13. The compound of any one of claims 1 to 12 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{6a1}, R^{6a2} are~~

~~independently selected from the group consisting of H; C_{1-6} alkyl; C_{2-6} alkenyl; C_{2-6} alkynyl; and A^{2a}, wherein C_{1-6} alkyl; C_{2-6} alkenyl; and C_{2-6} alkynyl are optionally substituted with one or more substituents selected from the group consisting of halogen; CN; OR^{6a3}; and A^{2a}, wherein the substituents are the same or different.~~

~~14~~11. The compound of ~~any one of~~ claim~~s 11 to 13~~10 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{6a} is C_{1-6} alkyl, optionally substituted with one or more halogen and/or one OR^{6a3} or R^{6a} is OR^{6a1} and R^{6a1} is preferably C_{1-6} alkyl, optionally substituted with one or more F and/or one OR^{6a3}, more preferably R^{6a1} is $CH_2CH_2CF_3$ or $CH_2CH_2OCF_3$, even more preferably $CH_2CH_2OCF_3$.

~~15~~12. The compound of any one of claims 1 to ~~10~~ 9 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^2 is A^{2a}.

~~16~~13. The compound of claim ~~15~~ 12 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^{2a} is phenyl~~;~~, cyclobutyl~~;~~, azetidinyl~~;~~, pyrrolidinyl~~;~~, or 5- to 6-membered aromatic heterocyclyl, preferably pyridyl, pyrazinyl, pyridazinyl, pyrazolyl or 1,2,4-oxadiazolyl, and wherein A^{2a} is optionally substituted with one or more R^6, which are the same or different.

~~17~~14. The compound of any one of claims 1 to ~~10~~9, ~~15~~12 and ~~16~~13 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^{2a} is substituted with one or two R^6, which are the same or different.

~~18~~15. The compound of any one of claims 1 to ~~10~~9, ~~15~~12 to ~~17~~14 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein each R^6 is independently F, Cl, CF_3, OCH_3, $OCHF_2$, OCF_3, CH_3, CH_2CH_3, CH_2CF_3, O-cyclopropyl, or cyclopropyl.

~~19~~16. The compound of any one of claims 1 to ~~18~~ 15 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^2 is CH_3~~;~~, F~~;~~, or H, preferably H.

~~20~~17. The compound of any one of claims 1 to ~~19~~ 16 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^3 is A^3.

~~21~~18. The compound of any one of claims 1 to ~~20~~ 17 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^3 is phenyl, pyridyl, pyrazinyl, pyrimidazyl, cyclopropyl, cyclobutyl or cyclohexyl, preferably phenyl, and wherein A^3 is optionally substituted with one or more R^{10}, which are the same or different.

~~22~~19. The compound of any one of claims 1 to ~~21~~ 18 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^3 is substituted with one, two or three, preferably one or two, more preferably two, R^{10}, which are the same or different.

~~23~~20. The compound of any one of claims 1 to 19~~22~~ or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^2 and R^3 are joined together with the oxygen and carbon atom to which they are attached to form a dihydrobenzopyran ring, wherein the ring is optionally substituted with one or more R^{10}, which are the same or different, preferably the ring is substituted with one or two R^{10}.

~~24~~21. The compound of any one of claims 1 to ~~23~~20 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{10} is independently F, Cl, Br, CN, CHF_2, CF_3, OCH_3, OCF_3, CH=O, CH_2OH or CH_3.

~~25~~22. The compound of any one of claims 1 to 21~~24~~ or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{a1} is H, or $C_{1\text{-}4}$ alkyl, wherein $C_{1\text{-}4}$ alkyl is optionally substituted with one or more substituents selected from the group consisting of halogen, OH, and O-$C_{1\text{-}3}$ alkyl, wherein the substituents are the same or different; preferably R^{a1} is H~~,~~; CH_3 or CH_2CH_3; more preferably R^{a1} is H.

~~26~~23. The compound of any one of claims 1 to ~~25~~ 22 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein the compound is

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-{5-[4-(trifluoromethyl)phenyl]-1,3,4-oxadiazol-2-yl}piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[4-(trifluoromethyl)phenyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chlorophenoxy)propanamido]-2-{5-[4-(trifluoromethyl)phenyl]-1,3,4-oxadiazol-2-yl}piperidine-1-carboxylate

2-(4-chlorophenoxy)-N-[(3S,6R)-6-{5-[4-(trifluoromethyl)phenyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]propanamide

N-[(3R,6S)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]-2-[(1s,3s)-3-(trifluoromethoxy)cyclobutoxy]acetamide

tert-butyl (2R,5S)-5-{2-[(6-chloro-5-fluoropyridin-3-yl)oxy]acetamido}-2-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-[(6-chloro-5-fluoropyridin-3-yl)oxy]-N-[(3S,6R)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(3,4-dichlorophenoxy)acetamido]-2-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}piperidine-1-carboxylate

2-(3,4-dichlorophenoxy)-N-[(3S,6R)-6-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-[3-chloro-4-(trifluoromethyl)phenoxy]-N-[(3S,6R)-6-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-[4-chloro-3-(difluoromethyl)phenoxy]-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-methylphenoxy)-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(3,4-dimethylphenoxy)-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]-2-{[6-(trifluoromethyl)pyridin-3-yl]oxy}acetamide

2-[3-methoxy-4-(trifluoromethyl)phenoxy]-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-2-fluorophenoxy)acetamido]-2-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-(4-chloro-2-fluorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(3-chloro-4-fluorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-[4-(trifluoromethyl)phenoxy]-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(3,4-dichlorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-2,3-difluorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3,5-difluorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-[3-fluoro-4-(trifluoromethyl)phenoxy]-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-2,2-difluoro-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-[3-chloro-4-(trifluoromethyl)phenoxy]-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(3,4,5-trichlorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-bromophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-[3-(trifluoromethyl)phenoxy]-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-cyanophenoxy)-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

~~tert-butyl (2R,4S)-4-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]pyrrolidine-1-carboxylate~~

~~2-(4-chloro-3-fluorophenoxy)-N-[(3S,5R)-5-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]pyrrolidin-3-yl]acetamide~~

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(6-methylpyridin-3-yl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6R)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

rac-2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-2-oxopiperidin-3-yl]acetamide

rac-2-(4-chloro-3-fluorophenoxy)-N-[(3R,6R)-2-oxo-6-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

tert-butyl (2S,5R)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-[5-(3,3,3-trifluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-{5-[3-(trifluoromethoxy)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-1-methylpiperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-1-methylpiperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-1-ethylpiperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-1-ethylpiperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-1-(2-methoxyethyl)piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

N-[(3S,6R)-6-[5-(5-chloro-1-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]-2-(4-chloro-3-fluorophenoxy)acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[6-(trifluoromethyl)pyridin-3-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(5-chloropyridin-2-yl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(4-chloro-3-fluorophenyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[3-(trifluoromethoxy)propyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-{5-[1-(2,2,2-trifluoroethyl)azetidin-3-yl]-1,3,4-oxadiazol-2-yl}piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[1-(2,2,2-trifluoroethyl)azetidin-3-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-[5-(3-cyclopropoxycyclobutyl)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3-cyclopropoxycyclobutyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(3,4-dichlorophenoxy)-N-[(3S,6R)-6-{5-[(1s,3s)-3-(difluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(trifluoromethoxy)methyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-[5-(3,3,3-trifluoro-2-methylpropoxy)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3,3,3-trifluoro-2-methylpropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(4,4,4-trifluorobutan-2-yl)oxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3,3-difluorobutoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(2,2-difluorocyclopropyl)methoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

N-[(3S,6R)-6-(5-butoxy-1,3,4-oxadiazol-2-yl)piperidin-3-yl]-2-(4-chloro-3-fluorophenoxy)acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(3,3-difluorocyclopentyl)oxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(2-cyclopropylethoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3-methylbutoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(2,2-difluorocyclobutyl)methoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3,3-difluorocyclobutoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(2,2,3,3,3-pentafluoropropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(4,4,4-trifluorobutoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[2-(difluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(pentyloxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3-methoxypropoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

~~2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(2-cyclopropoxyethoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide~~

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(2-ethoxyethoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

~~2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(2-cyclobutoxyethoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide~~

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(4,4-difluoropentyl)oxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(3,4-dichlorophenoxy)-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

~~N-[(3S,6R)-6-[5-(2-cyclopropoxyethoxy)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]-2-(3,4-dichlorophenoxy)acetamide~~

~~2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[2-(2,2-difluorocyclopropoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide~~

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-(5-{[2-(trifluoromethyl)cyclopropyl]methoxy}-1,3,4-oxadiazol-2-yl)piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-{5-[3-(trifluoromethyl)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[3-(trifluoromethyl)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[3-(trifluoromethoxy)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[3-(2,2,2-trifluoroethyl)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[3-methyl-3-(trifluoromethoxy)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

~~2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-(5-{methyl[2-(trifluoromethoxy)ethyl]amino}-1,3,4-oxadiazol-2-yl)piperidin-3-yl]acetamide~~

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(3-cyclopropoxyazetidin-1-yl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[3-(trifluoromethoxy)pyrrolidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-[2-(4-chloro-3-fluorophenoxy)acetamido]-2-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,2,4-oxadiazol-3-yl}piperidine-1-carboxylate

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(1s,3s)-3-(trifluoromethoxy)cyclobutyl]-1,2,4-oxadiazol-3-yl}piperidin-3-yl]acetamide

tert-butyl (2R,5S)-5-{2-[(6-chloro-5-fluoropyridin-3-yl)oxy]acetamido}-2-[5-(3,4-dichlorophenyl)-1,3,4-oxadiazol-2-yl]piperidine-1-carboxylate

2-[(6-chloro-5-fluoropyridin-3-yl)oxy]-N-[(3S,6R)-6-[5-(3,4-dichlorophenyl)-1,3,4-oxadiazol-2-yl]piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-1-methyl-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

~~2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-(5-{2-[(1R)-2,2-difluorocyclopropoxy]ethoxy}-1,3,4-oxadiazol-2-yl)piperidin-3-yl]acetamide~~

~~2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-(5-{2-[(1S)-2,2-difluorocyclopropoxy]ethoxy}-1,3,4-oxadiazol-2-yl)piperidin-3-yl]acetamide~~

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(1r,3r)-3-cyclopropoxycyclobutyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(1s,3s)-3-cyclopropoxycyclobutyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

(2R)-2-(4-chlorophenoxy)-N-[(3S,6R)-6-{5-[4-(trifluoromethyl)phenyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]propanamide

(2S)-2-(4-chlorophenoxy)-N-[(3S,6R)-6-{5-[4-(trifluoromethyl)phenyl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]propanamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-2-oxopiperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-2-oxopiperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(3S)-3-(trifluoromethoxy)pyrrolidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[(3R)-3-(trifluoromethoxy)pyrrolidin-1-yl]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide

N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]-2-[4-(trifluoromethyl)phenoxy]acetamide

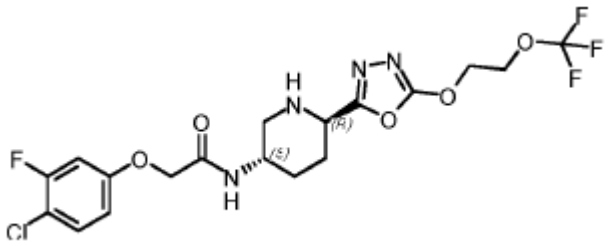
2-[3-chloro-4-(difluoromethyl)phenoxy]-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide or

2-[3-fluoro-4-(trifluoromethyl)phenoxy]-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide.

24. A compound or a pharmaceutically acceptable salt, solvate, hydrate, or tautomer thereof, wherein the compound is 2-(4-chloro-3-fluorophenoxy)-N-[(3S,6R)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide.

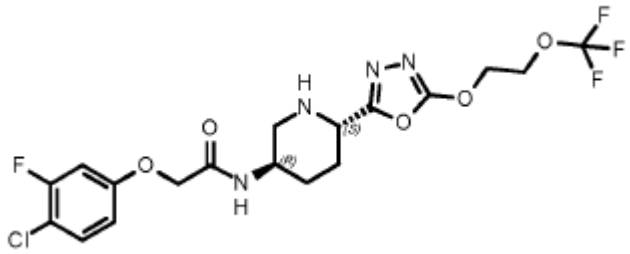
25. A compound or a pharmaceutically acceptable salt, solvate, hydrate, or tautomer thereof, wherein the compound is 2-(4-chloro-3-fluorophenoxy)-N-[(3R,6S)-6-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}piperidin-3-yl]acetamide.

26. A compound or a pharmaceutically acceptable salt, solvate, hydrate, or tautomer thereof, wherein the compound is



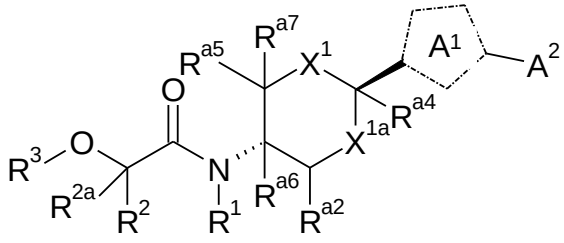
.

27. A compound or a pharmaceutically acceptable salt, solvate, hydrate, or tautomer thereof, wherein the compound is



.

~~27~~28. The compound of any one of claims 1 to ~~26~~27 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein the compound is of formula (Ia)



(Ia).

~~28. The compound of any one of claims 1 to 27 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof for use as a medicament.~~

29. A pharmaceutical composition comprising at least one compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined in any one of claims 1 to ~~27~~28 together with a pharmaceutically acceptable

carrier, optionally in combination with one or more other bioactive compounds or pharmaceutical compositions.

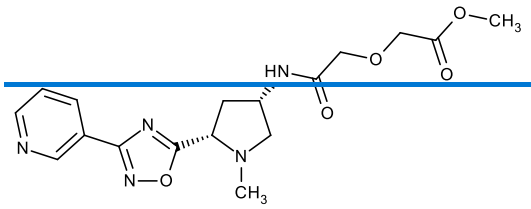
~~30. A compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined in any one of claims 1 to 27 or a pharmaceutical composition of claim 29 for use in treating or preventing of one or more diseases or disorders associated with integrated stress response.~~

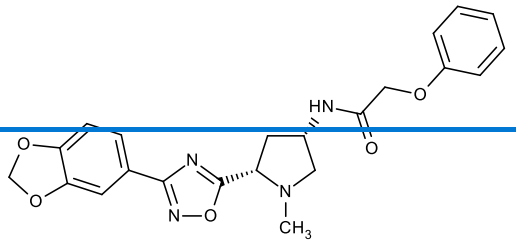
~~31. Use of a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined in any one of claims 1 to 27 or a pharmaceutical composition of claim 29 in the manufacture of a medicament for the treatment or prevention of one or more diseases or disorders associated with integrated stress response.~~

~~32~~30. Use of a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined in any one of claims 1 to ~~27~~28 or a pharmaceutical composition of claim 29 in the manufacture of a medicament for treating or preventing of one or more diseases or disorders selected from the group consisting of leukodystrophies, intellectual disability syndrome, neurodegenerative diseases and disorders, neoplastic diseases, infectious diseases, inflammatory diseases, musculoskeletal diseases, metabolic diseases, ocular diseases as well as diseases selected from the group consisting of organ fibrosis, chronic and acute diseases of the liver, chronic and acute diseases of the lung, chronic and acute diseases of the kidney, myocardial infarction, cardiovascular disease, arrhythmias, atherosclerosis, spinal cord injury, ischemic stroke, and neuropathic pain.

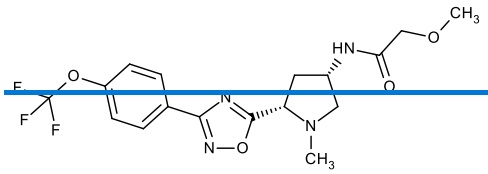
31. A compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined in any one of claims 1 to 28 or a pharmaceutical composition of claim 29 for use as a medicament.

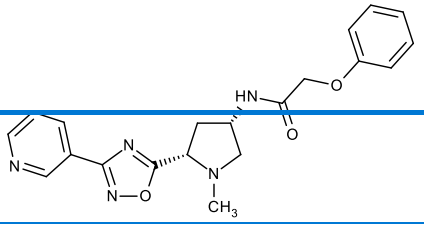
~~33. A compound as defined in any one of claims 1 to 27 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, provided that the following compounds or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof are excluded:~~



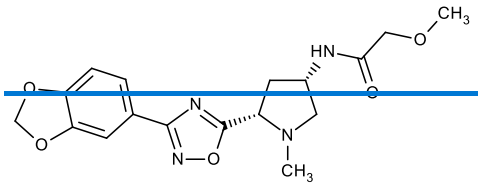


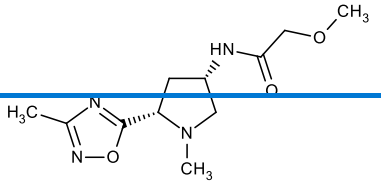
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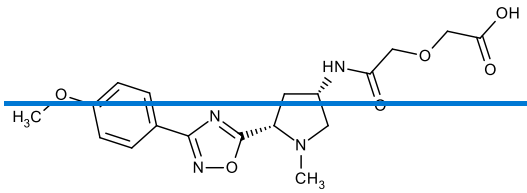


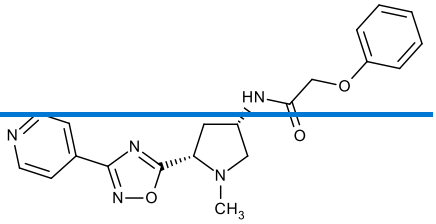
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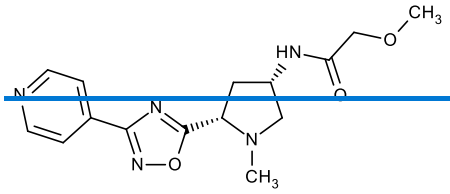


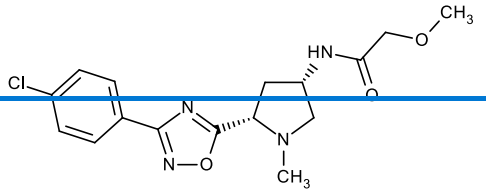
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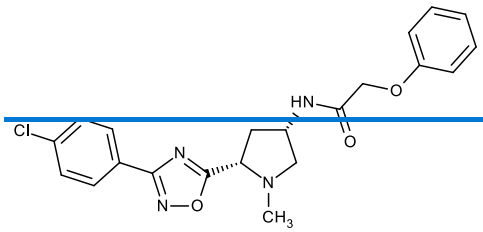


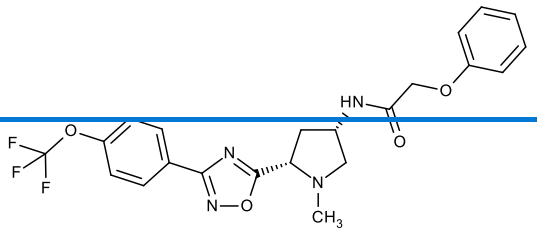
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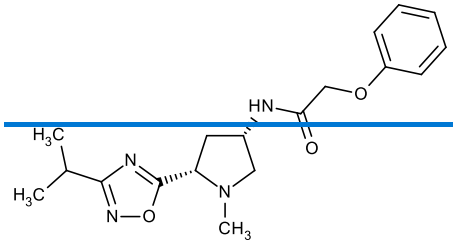


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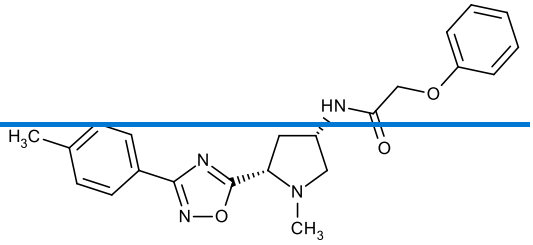




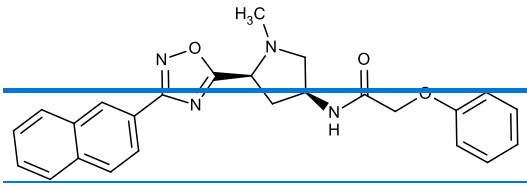
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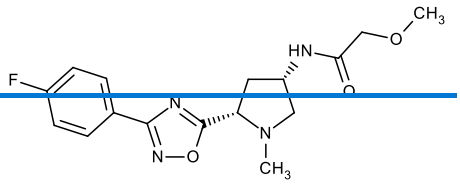
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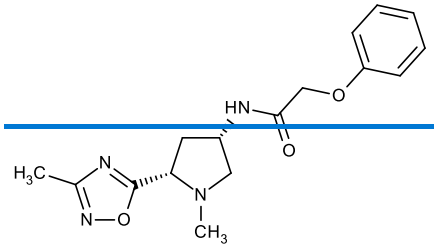
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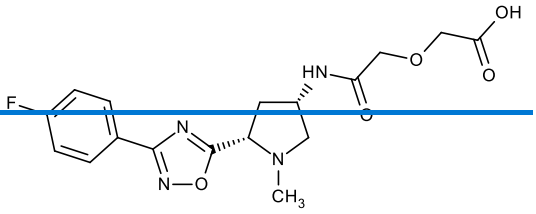
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~~CAS 1212561-17-5,~~



~~CAS 1212554-50-1,~~



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