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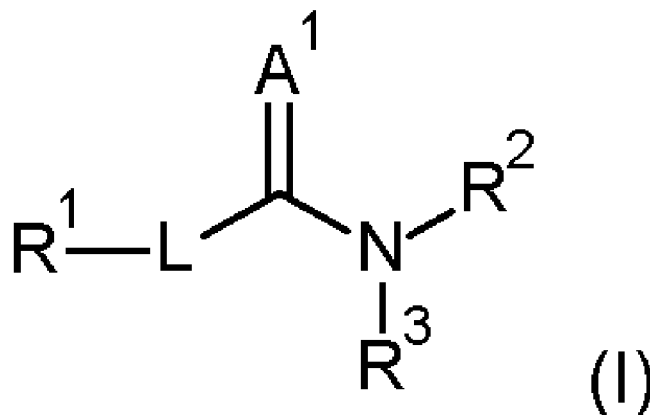
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(54) Title: SERINE BIOSYNTHETIC PATHWAY INHIBITORS



(57) Abstract: The present invention relates to a compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof as defined in claim 1 (I) the present invention also relates to a compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, as defined in the claims for use as a medicament, in particular for use in the prevention or treatment of a cellular proliferative disease.

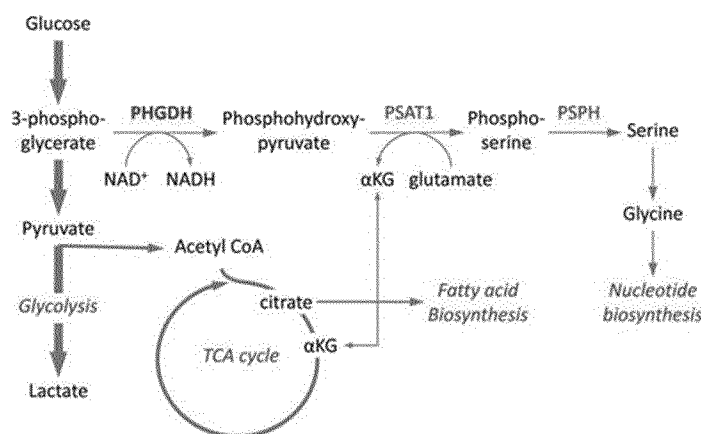
Serine biosynthetic pathway inhibitors

Field of the invention

The present invention relates to serine biosynthetic pathway inhibitors such as phosphoglycerate dehydrogenase inhibitors and phosphoserine aminotransferase 1 inhibitors, and to these inhibitors for use as a medicament, more in particular for the prevention or treatment of cellular proliferative disorders.

Background of the invention

There is an increased regain of interest for tumor metabolism. Recent advances in this field have shed light on how tumors fuel rapid growth by preferentially engaging biosynthetic pathways. Although cellular metabolic pathways are rich pickings for drug targets, pinpointing enzymes that critically contribute to tumor metabolism is key to establishing a therapeutic window since most of metabolic enzymes also play important roles in normal tissues. PHGDH (3-phosphoglycerate dehydrogenase) represents such ideal target for new anticancer strategies. This enzyme catalyzes the first step in the serine biosynthetic pathway (*Scheme 1*) with PHGDH (3-phosphoglycerate dehydrogenase), PSAT1 (phosphoserine aminotransferase 1) and PSPH (phosphoserine phosphatase) catalyzing the conversion of 3-phosphoglycerate into serine, together with the generation of NADH (reduced nicotinamide adenine dinucleotide) and α KG (α -ketoglutarate), the latter able to fuel the TCA (tricarboxylic acid) cycle.



Scheme 1

This pathway diverts a relatively small fraction of 3-phosphoglycerate from glycolysis to generate serine as well as equimolar amounts of NADH and α -ketoglutarate (α KG). The serine pathway was identified as a vital source of α KG to fuel the TCA cycle in a variety of tumor cells. Serine supplement could not rescue tumor cells in which PHGDH and PSAT1 genes were knocked down, thereby identifying the serine pathway as a process providing malignant cells with critical amounts of its intermediary synthetic products, α KG and possibly NADH, instead of the end product, serine (that may also be taken up from the extracellular fluid).

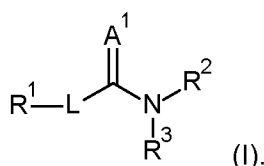
There are currently no tools to examine the role of the serine pathway and particularly of PHGDH and PSAT1 *in vivo*. Although much can be done *in vitro* using interfering RNA strategies, the *in vivo*

translation of these genetic models would underestimate the tumor biology and heterogeneity since the target genes will only be silenced in originally transduced cells. The resulting metabolic alterations strictly occurring in tumor cells will therefore not take into account that non-cancer cells located within the tumor, including macrophages, fibroblasts, immune cells and endothelial cells also represent major actors of the tumor metabolism.

There is therefore a need for finding and/or designing serine biosynthetic pathway inhibitors such as phosphoglycerate dehydrogenase inhibitors and/or phosphoserine aminotransferase 1 inhibitors which can be used in the prevention or treatment of cellular proliferative disorders.

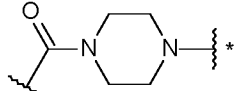
Summary of the invention

- 10 According to a first aspect of the present invention, a compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof as defined in claim 1 is provided



In particular a compound of formula (I), wherein

- 15 A^1 is selected from the group consisting of S; and O;

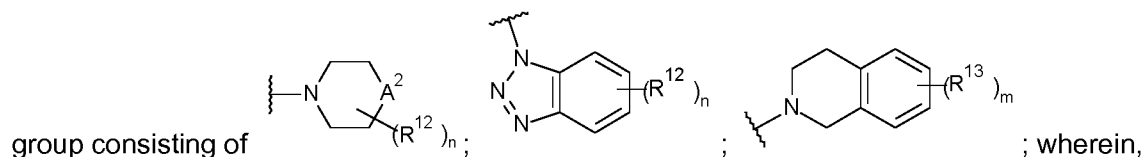
L is selected from the group consisting of $\text{C}=\text{O}$; S; NR^5 ; $^*\text{NR}^6\text{---NR}^7\text{---C}(\text{O})^{**}$; ** ; $\text{C}=\text{S}$; and a single bond; wherein * represents where L is bound to $\text{C}=\text{A}^1$; and ** represents where L is bound to R^1 ; and wherein,

- R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; 20 alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

- 25 R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from the



A² is selected from the group consisting of O; NR⁹; NH; CR¹⁰R¹¹; and S;

n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

R¹⁰ is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be unsubstituted or substituted with one or more Z⁵;

R¹¹ is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be unsubstituted or substituted with one or more Z⁶;

each R¹² is independently selected from the group consisting of hydrogen; halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two R¹² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹³ is independently selected from the group consisting of hydrogen; halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two R¹³ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

R⁵ is selected from the group consisting of hydrogen, alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁶ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

5 R⁷ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl;

10 heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least

15 one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

20 each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroarylheterocyclyl, heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z^2 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or
 5 two Z^2 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or
 10 two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or
 20 two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

25 each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or
 30 two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or
 35 two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl;

cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S,

N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl or aryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl or arylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH or S;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁹, O or S; R¹ is aryl; then L is not S;

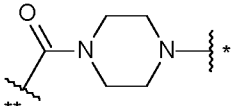
and with the proviso that said compound is not

- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(4-phenylphenyl)-2-thioxo-ethanone;
- 4-benzyl-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carbothioamide;
- (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-(4-fluorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-nitrophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-bromophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 1-morpholino-2-phenyl-ethanethione;

- N-phenylmorpholine-4-carboxamide;
- (4-phenylphenyl)-(4-phenylpiperazin-1-yl)methanethione;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 5 - 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-(4-methyl-1-piperidyl)-1-phenyl-2-thioxo-ethanone;
- 4-(2-morpholino-2-thioxo-acetyl)benzoic acid;
- 1-morpholino-2-phenyl-ethane-1,2-dione;
- 2-hydroxy-1-morpholino-2-phenyl-ethanone;
- 10 - N-morpholinobenzamide;
- 1-morpholino-3-phenyl-urea.

Preferably, the present invention relates to a compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, wherein,

A¹ is selected from the group consisting of S; and O;

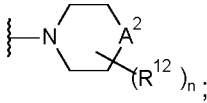
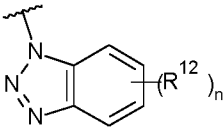
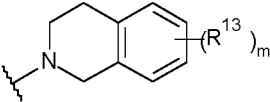
- 15 L is selected from the group consisting of C=O; S; NR⁵; *NR⁶-NR⁷-C(O)**; ;
C=S; and a single bond; wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹; and wherein,

- R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each
20 group can be unsubstituted or substituted with one or more Z¹;

R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

- R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl;
25 aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z³;

or R² and R³ form together with the nitrogen to which they are attached a moiety selected from

the group consisting of ; ; ;
wherein,

- 30 A² is selected from the group consisting of O; NR⁹; NH; CR¹⁰R¹¹; and S;
n is an integer selected from 0, 1, 2, or 3;
m is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

R^5 is selected from the group consisting of hydrogen, alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R⁶ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁷ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

5 each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

10 each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

15 or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; 20 wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at 25 least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and 30 heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroarylheterocyclyl, heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; - 35 C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z^2 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$;
 5 or two Z^2 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each Z^3 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$;
 10 or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each Z^4 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$;
 20 or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each Z^5 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^5 together with the atom to which they are attached can form
 25 a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each Z^6 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^6 together with the atom to which they are attached can form
 35 a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon

atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl or aryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl or arylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH or S;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁹, O or S; R¹ is aryl; then L is not S;

and with the proviso that said compound is not

- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(4-phenylphenyl)-2-thioxo-ethanone;
- 4-benzyl-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carbothioamide;
- (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-(4-fluorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-nitrophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-bromophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 1-morpholino-2-phenyl-ethanethione;

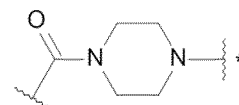
- N-phenylmorpholine-4-carboxamide;
- (4-phenylphenyl)-(4-phenylpiperazin-1-yl)methanethione;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 5 - 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-(4-methyl-1-piperidyl)-1-phenyl-2-thioxo-ethanone;
- 4-(2-morpholino-2-thioxo-acetyl)benzoic acid;
- 1-morpholino-2-phenyl-ethane-1,2-dione;
- 2-hydroxy-1-morpholino-2-phenyl-ethanone;
- 10 - N-morpholinobenzamide;
- 1-morpholino-3-phenyl-urea;
- 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(p-tolyl)-2-thioxo-ethanone;
- 15 - 2-(4-ethylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-cyclohexyl-2-oxo-2-phenyl-thioacetamide;
- 1-(3-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-ethoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 2-morpholino-1-(2-naphthyl)-2-thioxo-ethanone;
- 20 - 2-morpholino-1-(1-naphthyl)-2-thioxo-ethanone;
- 1-(2-furyl)-2-morpholino-2-thioxo-ethanone;
- 2-morpholino-1-(2-thienyl)-2-thioxo-ethanone;
- 1-(benzofuran-2-yl)-2-morpholino-2-thioxo-ethanone;
- 2-oxo-2-phenyl-N-(p-tolyl)thioacetamide;
- 25 - 2-oxo-N,2-diphenyl-thioacetamide;
- N-(4-fluorophenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-chlorophenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-bromophenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-isopropylphenyl)-2-oxo-2-phenyl-thioacetamide;
- 30 - N-(4-methoxyphenyl)-2-oxo-2-phenyl-thioacetamide;
- 2-oxo-N-phenyl-2-(p-tolyl)thioacetamide;
- N-[3-[2-(1-piperidyl)-2-thioxo-acetyl]phenyl]acetamide;
- 1-(5-chloro-2-phenoxy-phenyl)-2-morpholino-2-thioxo-ethanone;
- 1-[2-(4-chlorophenoxy)phenyl]-2-morpholino-2-thioxo-ethanone;
- 35 - methyl 4-(2-morpholino-2-thioxo-acetyl)benzoate;
- 1-(2-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 2-(2-chlorophenyl)-N,N-dimethyl-2-oxo-thioacetamide;
- 2-(4-chlorophenyl)-N,N-dimethyl-2-oxo-thioacetamide;
- N,N-dimethyl-2-(1-naphthyl)-2-oxo-thioacetamide;

- N-benzyl-N-methyl-2-oxo-2-phenyl-thioacetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
- 5 - N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

According to a second aspect, the present invention provides a pharmaceutical composition comprising one or more pharmaceutically acceptable excipients and a therapeutically effective amount of a compound according to the first aspect of the invention.

- 10 According to a third aspect, the present invention provides a compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use as a medicament, wherein,

A¹ is selected from the group consisting of S; O; and NR⁴;



L is selected from the group consisting of C=O; S; O; NR⁵; *NR⁶-NR⁷-C(O)**; ** ;

- 15 C=S; and a single bond; wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹; and wherein,

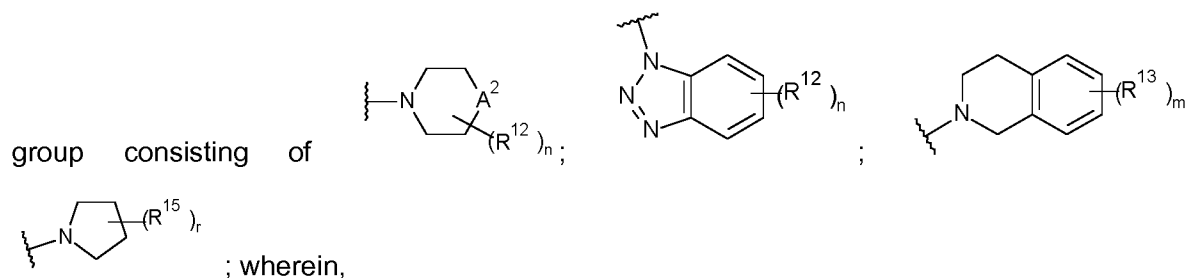
R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

- 20 R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein

- 25 each group can be unsubstituted or substituted with one or more Z³;

or R² and R³ form together with the nitrogen to which they are attached a moiety selected from the



A² is selected from the group consisting of O; NR⁹; CR¹⁰R¹¹; and S;

- 30 n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;

carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-\text{OR}^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{17} is independently selected from the group consisting of hydrogen; $-\text{NH}_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;

each R^{18} is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{19} is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl,

heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; heteroaryheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can

form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z³ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one

carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano;

hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

5 heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹;

carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -N

HS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached

can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one

carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be

10 oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano;

hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹;

carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -N

15 HS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached

can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one

carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be

oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

20 and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl or arylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

25

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

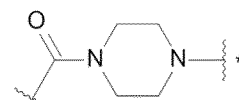
30 and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁹ or S; R¹ is aryl; then L is not S;

and with the proviso that said compound is not

- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 35 - (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) morpholine-4-carbodithioate;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;

- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 5 - 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone.

Preferably, the present invention relates to a compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use as a medicament, wherein, A^1 is selected from the group consisting of S; O; and NR^4 ;



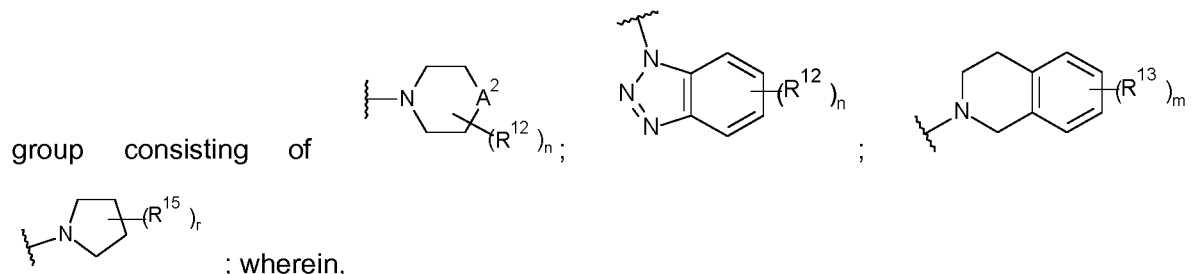
- 10 L is selected from the group consisting of $C=O$; S; O; NR^5 ; $*NR^6-NR^7-C(O)**$; $**$; $C=S$; and a single bond; wherein * represents where L is bound to $C=A^1$; and ** represents where L is bound to R^1 ; and wherein,

- R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group
15 can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

- R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl;
20 arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from the



- 25 A^2 is selected from the group consisting of O; NR^9 ; $CR^{10}R^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

- R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl;
30 arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl;

heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at

least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

R⁴ is selected from the group consisting of alkyl; hydroxyl; -OR¹⁸; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

5 R⁵ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁶ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

10 R⁷ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

15 each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

20 or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl;

25 wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

30 each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

35 each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z^1 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; heteroaryheterocyclyl, $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$;

- 5 each Z^2 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^2 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;
- 10

- each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;
- 15
- 20

- each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;
- 25

- each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;
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each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$;

$C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^7 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A^1 is O; R^1 is heteroaryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^1 is heteroarylalkyl or arylalkyl; A^2 is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is O; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is NR^9 or S; R^1 is aryl; then L is not S;

and with the proviso that said compound is not

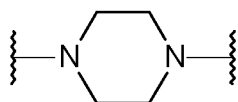
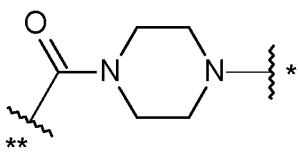
- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) morpholine-4-carbodithioate;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;

- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-[3-[2-(1-piperidyl)-2-thioxo-acetyl]phenyl]acetamide
- N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

According to a fourth aspect, the present invention provides a compound of formula (I), a
10 stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use in the
prevention or treatment of a cellular proliferative disease, wherein,

A¹ is selected from the group consisting of S; O; and NR⁴;

L is selected from the group consisting of C=O; S; O; NR⁵; *NR⁶-NR⁷-C(O)**; NR⁶-NR⁷.



; C=S; a single bond; C=NR⁸; and SO₂; wherein *

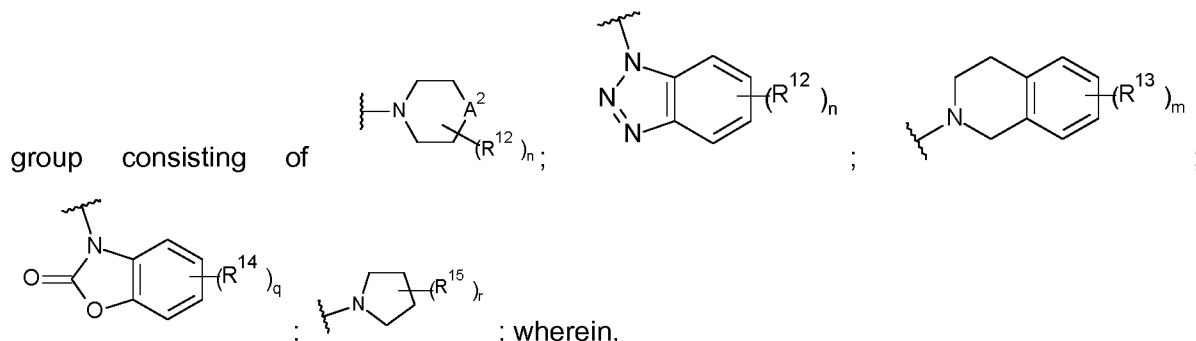
15 represents where L is bound to $C=A^1$; and ** represents where L is bound to R^1 ; and wherein,

R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclylalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z³;

25 or R² and R³ form together with the nitrogen to which they are attached a moiety selected from the



A^2 is selected from the group consisting of O; NR⁹; CR¹⁰R¹¹; and S;

n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

q is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each R^{14} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{14} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^8 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{17} is independently selected from the group consisting of hydrogen; $-NH_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;

each R^{18} is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{19} is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z^1 is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; heteroarylheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z^2 is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z^2 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z^3 is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z^4 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each Z^5 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each Z^6 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each Z^7 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A^1 is O; R^1 is heteroaryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^1 is heteroarylalkyl; A^2 is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

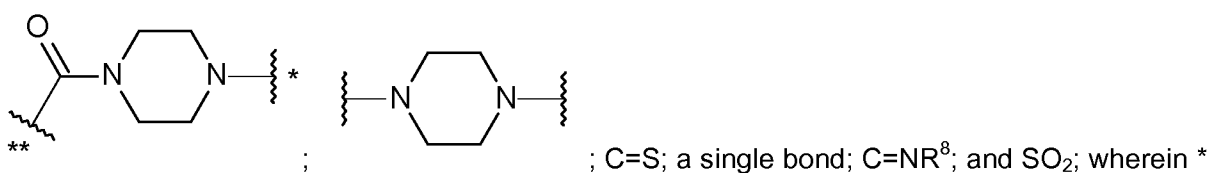
5 and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is O; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is NR^9 ; R^1 is aryl; then L is not S.

Preferably, the present invention relates to a compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use in the prevention or treatment
10 of a cellular proliferative disease, wherein,

A^1 is selected from the group consisting of S; O; and NR^4 ;

L is selected from the group consisting of $C=O$; S; O; NR^5 ; $*NR^6-NR^7-C(O)**$; NR^6-NR^7 ;



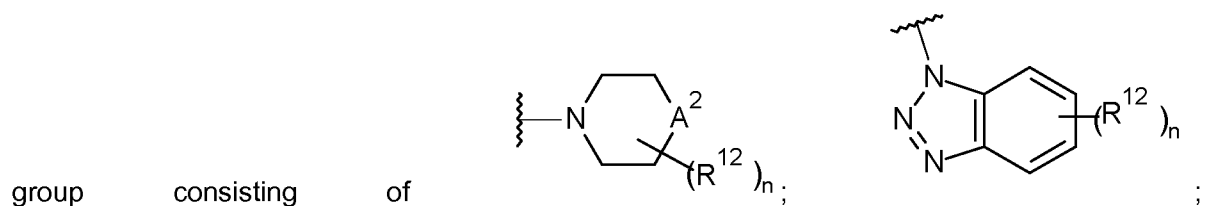
15 represents where L is bound to $C=A^1$; and ** represents where L is bound to R^1 ; and wherein,

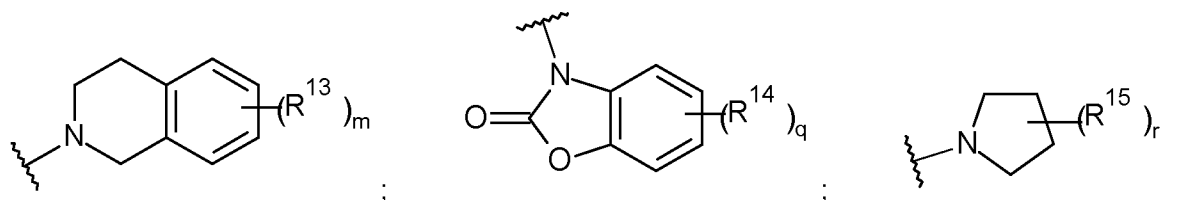
R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein
20 each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

25 or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from the





wherein,

A^2 is selected from the group consisting of O; NR^9 ; $CR^{10}R^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

5 m is an integer selected from 0, 1, 2, or 3;

q is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{14} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{14} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^8 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at

least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; heteroarylheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl;

5 heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkoxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkoxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkoxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^7 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkoxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl; A² is O, then L is not a single bond;

5 and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

10 and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁹; R¹ is aryl; then L is not S;

and with the proviso that said compound is not

2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;

15 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;

N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;

N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;

N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;

N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

20 The present invention also provides a pharmaceutical composition according to the second aspect of the invention for use in the prevention or treatment of a cellular proliferative disease.

The present invention also provides a method of treatment of a cellular proliferative disease, comprising administering to a subject in need thereof an effective amount of a compound according to the first aspect of the invention, or a pharmaceutical composition according to the second aspect
25 of the invention.

The present invention also provides a method for inhibiting serine biosynthesis comprising the step of contacting at least one enzyme of the serine biosynthetic pathway with an effective amount of a compound according to the first aspect of the invention, or as defined in the fourth aspect of the invention. In some embodiment, said at least one enzyme of the serine biosynthetic pathway is
30 selected from the group comprising phosphoglycerate dehydrogenase and phosphoserine aminotransferase 1.

The present invention also provides a method for inhibiting phosphoglycerate dehydrogenase comprising contacting said phosphoglycerate dehydrogenase with an effective amount of a compound according to the first aspect of the invention, or as defined in the fourth aspect of the
35 invention.

The present invention also encompasses the combined use of a compound according to the first aspect of the invention, or as defined in the fourth aspect of the invention, together with an immune checkpoint inhibitor. Immune checkpoint inhibitors are described in e.g. WO2017011666, IMS health Institute global Oncology report June 2016, Nature Reviews Clinical Oncology 2013 (13) 143-158, and Clin. Cancer research 2013 (19) 1021-1034. Examples of Immune check point targets as provided in the aforementioned literature comprise : PD1, PD-L1, CTLA4, IDO, TDO, CD122, CD27, G1TR, CD40, OX40, CD73, CD137, 4-1BB, CSF1R, LAG3, KIR, TIM-3, IL2, ADA, STING and TIGIT. The person skilled in the art will understand the advantage of combining the compounds of present invention with an immune check point inhibitor. The compounds of the present invention may also be given in combination with CAR-T cell therapeutic strategy. Combination of the compounds comprises either the administration of the compound of the present invention prior to immune checkpoint therapy, administration concomittant with immune checkpoint therapy, or administration after immune checkpoint therapy. The person skilled in the art will know how to combine the respective compounds.

In any of the aspects of the invention, the cellular proliferative disorder may be cancer (e.g., breast cancer, prostate cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, vulval cancer, thyroid cancer, hepatic carcinoma, gastric cancer, melanoma, or neck cancer). The independent and dependent claims and statements set out particular and preferred features of the invention. Features from the dependent claims and statements may be combined with features of the independent or other dependent claims and statement as appropriate.

The present invention will now be further described. In the following passages, different aspects of the invention are defined in more detail. Each aspect so defined may be combined with any other aspect or aspects unless clearly indicated to the contrary. In particular, any feature indicated as being preferred or advantageous may be combined with any other feature or features indicated as being preferred or advantageous.

Brief description of the figures

Figure 1 represents in Section (A) a graph plotting fluorescence intensity, as a function of time at different PHGDH concentrations. Section (B) is a graph plotting fluorescence intensity, as a function of time at different PHGDH concentrations. Section (C) is a graph plotting fluorescence intensity, as a function of time at different PHGDH concentrations. Section (D) is a graph plotting fluorescence intensity, as a function of time at different PHGDH concentrations.

Figure 2 represents a graph plotting the cell density as a function of compound 40 concentration for BT20 and MDA-MB-231 cell lines.

Figure 3 represents a graph plotting the cell density as a function of compound 40 concentration for in presence of absence of serine.

Figure 4 represents in Sections (A) and (C) a representative immunoblot for PHGDH. Section (B) is a graph plotting cell density (for 5 days) of SiHa and MDA-MB-231 cells in either serine-replete
5 (+Ser) or serine-deplete (–Ser) medium. Data are shown as mean $\pm$ SEM ($n \geq 3$). Section (D) is a graph plotting cell density (for 5 days) of shScr and shPHGDH cells in either serine-replete (+Ser) or serine-deplete (–Ser) medium. Data are shown as mean $\pm$ SEM ($n \geq 3$).

Detailed description of the invention

Before the present invention is described, it is to be understood that this invention is not limited to
10 particular compounds, uses, and method described, as such compounds, uses, and methods may, of course, vary. It is also to be understood that the terminology used herein is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

When describing the compounds and processes of the invention, the terms used are to be construed in accordance with the following definitions, unless a context dictates otherwise.

15 As used in the specification and the appended claims, the singular forms "a", "an," and "the" include both singular and plural referents unless the context clearly dictates otherwise. By way of example, "a compound" means one compound or more than one compound.

The terms "comprising", "comprises" and "comprised of" as used herein are synonymous with "including", "includes" or "containing", "contains", and are inclusive or open-ended and do not
20 exclude additional, non-recited members, elements or method steps. The terms "comprising", "comprises" and "comprised of" also include the term "consisting of".

The term "about" as used herein when referring to a measurable value such as a parameter, an amount, a temporal duration, and the like, is meant to encompass variations of $\pm 10\%$ or less, preferably $\pm 5\%$ or less, more preferably $\pm 1\%$ or less, and still more preferably $\pm 0.1\%$ or less of
25 and from the specified value, insofar such variations are appropriate to perform in the disclosed invention. It is to be understood that the value to which the modifier "about" refers is itself also specifically, and preferably, disclosed.

As used herein, the term "and/or," when used in a list of two or more items, means that any one of the listed items can be employed by itself or any combination of two or more of the listed items can
30 be employed. For example, if a list is described as comprising group A, B, and/or C, the list can comprise A alone; B alone; C alone; A and B in combination; A and C in combination, B and C in combination; or A, B, and C in combination.

The recitation of numerical ranges by endpoints includes all integer numbers and, where appropriate, fractions subsumed within that range (e.g. 1 to 5 can include 1, 2, 3, 4 when referring to,
35 for example, a number of elements, and can also include 1.5, 2, 2.75 and 3.80, when referring to, for example, measurements). The recitation of end points also includes the end point values themselves

(e.g. from 1.0 to 5.0 includes both 1.0 and 5.0). Any numerical range recited herein is intended to include all sub-ranges subsumed therein.

Reference throughout this specification to “one embodiment” or “an embodiment” means that a particular feature, structure or characteristic described in connection with the embodiment is included in at least one embodiment of the present invention. Thus, appearances of the phrases “in one embodiment” or “in an embodiment” in various places throughout this specification are not necessarily all referring to the same embodiment, but may. Furthermore, the particular features, structures or characteristics may be combined in any suitable manner, as would be apparent to a person skilled in the art from this disclosure, in one or more embodiments. Furthermore, while some embodiments described herein include some but not other features included in other embodiments, combinations of features of different embodiments are meant to be within the scope of the invention, and form different embodiments, as would be understood by those in the art. For example, in the following claims, any of the claimed embodiments can be used in any combination.

Unless otherwise defined, all terms used in disclosing the invention, including technical and scientific terms, have the meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. By means of further guidance, definitions for the terms used in the description are included to better appreciate the teaching of the present invention.

When describing the present invention, the terms used are to be construed in accordance with the following definitions, unless a context dictates otherwise.

The terms described above and others used in the specification are well understood to those in the art.

Whenever the term “substituted” is used herein, it is meant to indicate that one or more hydrogen atoms on the atom indicated in the expression using “substituted” is replaced with a selection from the indicated group, provided that the indicated atom’s normal valence is not exceeded, and that the substitution results in a chemically stable compound, i.e. a compound that is sufficiently robust to survive isolation from a reaction mixture.

Where groups can be substituted, such groups may be substituted with one or more, and preferably one, two or three substituents. Preferred substituents may be selected from but not limited to, for example, the group comprising halo, hydroxyl, alkyl, alkoxy, haloalkyl, haloalkyloxy, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, alkylthio, cyano, amino, nitro, carboxyl, aminocarbonyl, hydroxycarbonylalkyl, alkyloxycarbonyl, mono- or dialkylamino, mono- or dialkylaminocarbonyl, alkylcarbonyl, -S(O)alkyl, -S(O)₂alkyl, alkylcarbonylamino, and mono or di-alkylaminocarbonylalkyl.

The terminology regarding a chemical group “wherein at least one carbon atom or heteroatom of said group can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂” as used herein, refers to a group where two or more hydrogen atoms on a carbon atom or heteroatom of said group are taken together to form C=O, C=S, N=O, N=S, S=O or S(O)₂. As an example, the terminology “an alkyl wherein a carbon atom or heteroatom of said alkyl can be oxidized to form a C=O, C=S, N=O, N=S, S=O or S(O)₂”, includes among other examples CH₃-C(O)-CH₂-, CH₃-C(O)-, CH₃-

C(S)-CH₂- and (CH₃)₂-CH₂-C(O)-CH₂-CH₂-. For example, the terminology "a 5-, 6-, or 7-membered heterocyclyl wherein a carbon atom or heteroatom of said heterocyclyl can be oxidized to form a C=O, C=S, N=O, N=S, S=O or S(O)₂", includes among other examples 6-oxo-1H-pyridin-3-yl, 2-oxo-1H-pyridin-4yl, 6-thioxo-1H-pyridin-3-yl and 2-thioxo-1H-pyridin-4yl.

- 5 The term "halo" or "halogen" as a group or part of a group is generic for fluoro, chloro, bromo, iodo.

The term "amino" refers to the group -NH₂.

The term "hydroxyl" or "hydroxy" as used herein refers to the group -OH.

The term "thiol" or "sulfuhydriyl" refers to the group -SH.

The term "oxo" as used herein refers to the group =O.

- 10 The term "nitro" as used herein refers to the group -NO₂.

The term "cyano" as used herein refers to the group -CN.

The term "carboxy" or "carboxyl" or "hydroxycarbonyl" as used herein refers to the group -CO₂H.

The term "aminocarbonyl" as used herein refers to the group -CO-NH₂.

- The term "alkyl" as a group or part of a group, refers to a hydrocarblyl group of formula C_nH_{2n+1} wherein n is a number greater than or equal to 1. Alkyl groups may be linear or branched and may be substituted as indicated herein. Generally, alkyl groups of this invention comprise from 1 to 6 carbon atoms, preferably from 1 to 5 carbon atoms, preferably from 1 to 4 carbon atoms, more preferably from 1 to 3 carbon atoms, still more preferably 1 to 2 carbon atoms. When a subscript is used herein following a carbon atom, the subscript refers to the number of carbon atoms that the named group may contain. For example, the term "C₁₋₆alkyl", as a group or part of a group, refers to a hydrocarblyl group of formula -C_nH_{2n+1} wherein n is a number ranging from 1 to 6. Thus, for example, "C₁₋₆alkyl" includes all linear or branched alkyl groups with between 1 and 6 carbon atoms, and thus includes methyl, ethyl, n-propyl, i-propyl, butyl and its isomers (e.g. n-butyl, i-butyl and t-butyl); pentyl and its isomers, hexyl and its isomers. For example, "C₁₋₅alkyl" includes all includes all linear or branched alkyl groups with between 1 and 5 carbon atoms, and thus includes methyl, ethyl, n-propyl, i-propyl, butyl and its isomers (e.g. n-butyl, i-butyl and t-butyl); pentyl and its isomers. For example, "C₁₋₄alkyl" includes all linear or branched alkyl groups with between 1 and 4 carbon atoms, and thus includes methyl, ethyl, n-propyl, i-propyl, butyl and its isomers (e.g. n-butyl, i-butyl and t-butyl). For example "C₁₋₃alkyl" includes all linear or branched alkyl groups with between 1 and 3 carbon atoms, and thus includes methyl, ethyl, n-propyl, i-propyl. A "substituted alkyl" refers to an alkyl group substituted with one or more substituent(s) (for example 1 to 3 substituent(s), for example 1, 2, or 3 substituent(s)) at any available point of attachment.

- When the suffix "ene" is used in conjunction with an alkyl group, i.e. "alkylene", this is intended to mean the alkyl group as defined herein having two single bonds as points of attachment to other groups. As used herein, the term "alkylene", by itself or as part of another substituent, refers to alkyl groups that are divalent, i.e., with two single bonds for attachment to two other groups. Alkylene groups may be linear or branched and may be substituted as indicated herein. Non-limiting

examples of alkylene groups include methylene (-CH₂-), ethylene (-CH₂-CH₂-), methylenemethylene (-CH(CH₃)-), 1-methyl-ethylene (-CH(CH₃)-CH₂-), n-propylene (-CH₂-CH₂-CH₂-), 2-methylpropylene (-CH₂-CH(CH₃)-CH₂-), 3-methylpropylene (-CH₂-CH₂-CH(CH₃)-), n-butylene (-CH₂-CH₂-CH₂-CH₂-), 2-methylbutylene (-CH₂-CH(CH₃)-CH₂-CH₂-), 4-methylbutylene (-CH₂-CH₂-CH₂-CH(CH₃)-), pentylene
 5 and its chain isomers, hexylene and its chain isomers.

When the term "alkyl" is used as a suffix following another term, as in "hydroxyalkyl," this is intended to refer to an alkyl group, as defined above, being substituted with one or two (preferably one) substituent(s) selected from the other, specifically-named group, also as defined herein. The term "hydroxyalkyl" therefore refers to a -R^a-OH group wherein R^a is alkylene as defined herein.

10 The term "haloalkyl" as a group or part of a group, refers to an alkyl group having the meaning as defined above wherein one, two, or three hydrogen atoms are each replaced with a halogen as defined herein. Non-limiting examples of such haloalkyl groups include chloromethyl, 1-bromoethyl, fluoromethyl, difluoromethyl, trifluoromethyl, 1,1,1-trifluoroethyl, trichloromethyl, tribromomethyl, and the like.

15 The term "trihalomethyl" as a group or part of a group, refers to a C₁ alkyl group (methyl) having the meaning as defined above wherein three hydrogen atoms are each replaced with a halogen as defined herein. Non-limiting examples of such trihalomethyl groups include trichloromethyl, tribromomethyl, and the like.

The term "alkoxy" or "alkyloxy", as a group or part of a group, refers to a group having the formula -
 20 OR^b wherein R^b is C₁₋₆alkyl as defined herein above. Non-limiting examples of suitable alkoxy include methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy, tert-butoxy, pentyloxy and hexyloxy.

The term "haloalkoxy", as a group or part of a group, refers to a group of formula -O-R^c wherein R^c is haloC₁₋₆alkyl as defined herein. Non-limiting examples of suitable haloC₁₋₆alkoxy include
 25 fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, 1,1,2,2-tetrafluoroethoxy, 2-fluoroethoxy, 2-chloroethoxy, 2,2-difluoroethoxy, 2,2,2-trichloroethoxy, trichloromethoxy, 2-bromoethoxy, pentafluoroethyl, 3,3,3-trichloropropoxy, 4,4,4-trichlorobutoxy.

The term "alkenyl" as a group or part of a group, refers to an unsaturated hydrocarbyl group, which may be linear, or branched, comprising one or more carbon-carbon double bonds. When a subscript
 30 is used herein following a carbon atom, the subscript refers to the number of carbon atoms that the named group may contain. For example, the term "alkenyl" refers to an unsaturated hydrocarbyl group, which may be linear, or branched comprising one or more carbon-carbon double bonds and comprising from 2 to 6 carbon atoms. For example, C₂₋₄alkenyl includes all linear, or branched alkenyl groups having 2 to 4 carbon atoms. Examples of C₂₋₆alkenyl groups are ethenyl, 2-propenyl,
 35 2-butenyl, 3-butenyl, 2-pentenyl and its isomers, 2-hexenyl and its isomers, 2,4-pentadienyl, and the like.

Where alkenyl groups as defined herein are divalent groups having single bonds for attachment to two other groups, they are termed "alkenylene". As used herein, the term "alkenylene", by itself or as

part of another substituent, refers to alkenyl groups that are divalent, i.e., with two single bonds for attachment to two other groups.

The term "alkenyloxy", as a group or part of a group, refers to a group having the formula $-OR^d$ wherein R^d is alkenyl as defined herein above.

- 5 The term "alkynyl" as a group or part of a group, refers to an unsaturated hydrocarbyl group, which may be linear, or branched, comprising one or more carbon-carbon triple bonds. When a subscript is used herein following a carbon atom, the subscript refers to the number of carbon atoms that the named group may contain. For example, the term " C_{2-6} alkynyl" refers to an unsaturated hydrocarbyl group, which may be linear, or branched comprising one or more carbon-carbon triple bonds and
- 10 comprising from 2 to 6 carbon atoms. For example, C_{2-4} alkynyl includes all linear, or branched alkynyl groups having 2 to 4 carbon atoms. Non limiting examples of C_{2-6} alkynyl groups include ethynyl, 2-propynyl, 2-butylnyl, 3-butylnyl, 2-pentylnyl and its chain isomers, 2-hexynyl and its chain isomers, and the like.

Where alkynyl groups as defined herein are divalent groups having single bonds for attachment to

15 two other groups, they are termed "alkynylene". As used herein, the term "alkynylene", by itself or as part of another substituent, refers to alkynyl groups that are divalent, i.e., with two single bonds for attachment to two other groups.

The term "alkynyloxy", as a group or part of a group, refers to a group having the formula $-OR^e$ wherein R^e is alkynyl as defined herein above.

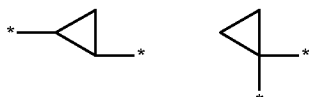
- 20 The term "cycloalkyl", as a group or part of a group, refers to a cyclic alkyl group, that is a monovalent, saturated, hydrocarbyl group having 1 or more cyclic structure, and comprising from 3 to 12 carbon atoms, more preferably from 3 to 10 carbon atoms, more preferably from 3 to 8 carbon atoms; more preferably from 3 to 6 carbon atoms. Cycloalkyl includes all saturated hydrocarbon groups containing 1 or more rings, including monocyclic, bicyclic groups or tricyclic. The further rings
- 25 of multi-ring cycloalkyls may be either fused, bridged and/or joined through one or more spiro atoms. When a subscript is used herein following a carbon atom, the subscript refers to the number of carbon atoms that the named group may contain. For example, the term " C_{3-12} cycloalkyl", a cyclic alkyl group comprising from 3 to 12 carbon atoms. For example, the term " C_{3-10} cycloalkyl", a cyclic alkyl group comprising from 3 to 10 carbon atoms. For example, the term " C_{3-8} cycloalkyl", a cyclic
- 30 alkyl group comprising from 3 to 8 carbon atoms. For example, the term " C_{3-6} cycloalkyl", a cyclic alkyl group comprising from 3 to 6 carbon atoms. Examples of C_{3-12} cycloalkyl groups include but are not limited to adamantyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicycle[2.2.1]heptan-2-yl, (1S,4R)-norbornan-2-yl, (1R,4R)-norbornan-2-yl, (1S,4S)-norbornan-2-yl, (1R,4S)-norbornan-2-yl.

- 35 When the suffix "ene" is used in conjunction with a cycloalkyl group, i.e. cycloalkylene, this is intended to mean the cycloalkyl group as defined herein having two single bonds as points of attachment to other groups. Non-limiting examples of "cycloalkylene" include 1,2-cyclopropylene,

1,1-cyclopropylene, 1,1-cyclobutylene, 1,2-cyclobutylene, 1,3-cyclopentylene, 1,1-cyclopentylene, and 1,4-cyclohexylene.

Where an alkylene or cycloalkylene group is present, connectivity to the molecular structure of which it forms part may be through a common carbon atom or different carbon atom. To illustrate this

5 applying the asterisk nomenclature of this invention, a C₃alkylene group may be for example *-CH₂CH₂CH₂-, *-CH(-CH₂CH₃)-* or *-CH₂CH(-CH₃)-*. Likewise a C₃cycloalkylene group may be



The term “aryl”, as a group or part of a group, refers to a polyunsaturated, aromatic hydrocarbonyl group having a single ring (i.e. phenyl) or multiple aromatic rings fused together (e.g. naphthyl), or
 10 linked covalently, typically containing 6 to 12 atoms; preferably 6 to 10, wherein at least one ring is aromatic. The aromatic ring may optionally include one to two additional rings (either cycloalkyl, heterocyclyl or heteroaryl) fused thereto. Examples of suitable aryl include C₆₋₁₂aryl, preferably C₆₋₁₀aryl, more preferably C₆₋₈aryl. Non-limiting examples of aryl comprise phenyl, biphenyl, biphenylenyl, or 1-or 2-naphthanylenyl; 1-, 2-, 3-, 4-, 5- or 6-tetralinyl (also known as “1,2,3,4-
 15 tetrahydronaphthalene); 1-, 2-, 3-, 4-, 5-, 6-, 7- or 8-azulenyl, 4-, 5-, 6 or 7-indenyl; 4- or 5-indanyl; 5-, 6-, 7- or 8-tetrahydronaphthyl; 1,2,3,4-tetrahydronaphthyl; and 1,4-dihydronaphthyl; 1-, 2-, 3-, 4- or 5-pyrenyl. A “substituted aryl” refers to an aryl group having one or more substituent(s) (for example 1, 2 or 3 substituent(s), or 1 to 2 substituent(s)), at any available point of attachment.

As used herein, the term “spiro atom” refers to the atom that connects two cyclic structures in a spiro
 20 compound. Non limiting examples of spiro atoms include quaternary carbon atoms. As used herein, the term “spiro compound” refers to a bicyclic compound wherein the two rings are connected through one atom.

When the suffix “ene” is used in conjunction with an aryl group; i.e. arylene, this is intended to mean the aryl group as defined herein having two single bonds as points of attachment to other groups.
 25 Suitable “arylene” groups include 1,4-phenylene, 1,2-phenylene, 1,3-phenylene, biphenylene, naphthylene, indenylene, 1-, 2-, 5- or 6-tetralinylene, and the like. Where a carbon atom in an aryl group is replaced with a heteroatom, the resultant ring is referred to herein as a heteroaryl ring.

The term “aryloxy”, as a group or part of a group, refers to a group having the formula -OR^g wherein R^g is aryl as defined herein above.

30 The term “arylalkyl”, as a group or part of a group, means a alkyl as defined herein, wherein at least one hydrogen atom is replaced by at least one aryl as defined herein. Non-limiting examples of arylalkyl group include benzyl, phenethyl, dibenzylmethyl, methylphenylmethyl, 3-(2-naphthyl)-butyl, and the like.

The term “arylalkyloxy”, as a group or part of a group, refers to a group having the formula -O-R^a-R^g
 35 wherein R^g is aryl, and R^a is alkylene as defined herein above.

The terms "heterocyclyl" or "heterocycloakyl" or "heterocyclo", as a group or part of a group, refer to non-aromatic, fully saturated or partially unsaturated cyclic groups (for example, 3 to 7 member monocyclic, 7 to 11 member bicyclic, or comprising a total of 3 to 10 ring atoms) which have at least one heteroatom in at least one carbon atom-containing ring; wherein said ring may be fused to an aryl, cycloalkyl, heteroaryl or heterocyclyl ring. Each ring of the heterocyclyl group containing a heteroatom may have 1, 2, 3 or 4 heteroatoms selected from N, O and/or S, where the N and S heteroatoms may optionally be oxidized and the N heteroatoms may optionally be quaternized, and wherein at least one carbon atom of heterocyclyl can be oxidized to form at least one C=O. The heterocyclic group may be attached at any heteroatom or carbon atom of the ring or ring system, where valence allows. The rings of multi-ring heterocycles may be fused, bridged and/or joined through one or more spiro atoms.

Non limiting exemplary heterocyclic groups include aziridinyl, oxiranyl, thiiranyl, piperidinyl, azetidiny, oxetanyl, pyrrolidinyl, thietanyl, 2-imidazolinyl, pyrazolidinyl, imidazolidinyl, isoxazolinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, piperidinyl, succinimidyl, 3H-indolyl, indoliny, chromanyl (also known as 3,4-dihydrobenzo[b]pyranyl), isoindoliny, 2H-pyrrolyl, 1-pyrroliny, 2-pyrroliny, 3-pyrroliny, 4H-quinoliziny, 2-oxopiperazinyl, piperazinyl, homopiperazinyl, 2-pyrazolinyl, 3-pyrazolinyl, tetrahydro-2H-pyranyl, 2H-pyranyl, 4H-pyranyl, 3,4-dihydro-2H-pyranyl, 3-dioxolanyl, 1,4-dioxanyl, 2,5-dioximidazolidinyl, 2-oxopiperidinyl, 2-oxopyrrolodiny, indoliny, tetrahydropyranyl, tetrahydrofuranyl, tetrahydrothiophenyl, tetrahydroquinoliny, tetrahydroisoquinolin-1-yl, tetrahydroisoquinolin-2-yl, tetrahydroisoquinolin-3-yl, tetrahydroisoquinolin-4-yl, thiomorpholin-4-yl, thiomorpholin-4-ylsulfoxide, thiomorpholin-4-ylsulfone, 1,3-dioxolanyl, 1,4-oxathianyl, 1,4-dithianyl, 1,3,5-trioxanyl, 1H-pyrroliziny, tetrahydro-1,1-dioxothiophenyl, N- formylpiperazinyl, and morpholin-4-yl. The term "aziridinyl" as used herein includes aziridin-1-yl and aziridin-2-yl. The term "oxyranyl" as used herein includes oxyranyl-2-yl. The term "thiiranyl" as used herein includes thiiran-2-yl. The term "azetidiny" as used herein includes azetidin-1-yl, azetidin-2-yl and azetidin-3-yl. The term "oxetanyl" as used herein includes oxetan-2-yl and oxetan-3-yl. The term "thietanyl" as used herein includes thietan-2-yl and thietan-3-yl. The term "pyrrolidinyl" as used herein includes pyrrolidin-1-yl, pyrrolidin-2-yl and pyrrolidin-3-yl. The term "tetrahydrofuranyl" as used herein includes tetrahydrofuran-2-yl and tetrahydrofuran-3-yl. The term "tetrahydrothiophenyl" as used herein includes tetrahydrothiophen-2-yl and tetrahydrothiophen-3-yl. The term "succinimidyl" as used herein includes succinimid-1-yl and succinimid-3-yl. The term "dihydropyrrolyl" as used herein includes 2,3-dihydropyrrol-1-yl, 2,3-dihydro-1H-pyrrol-2-yl, 2,3-dihydro-1H-pyrrol-3-yl, 2,5-dihydropyrrol-1-yl, 2,5-dihydro-1H-pyrrol-3-yl and 2,5-dihydropyrrol-5-yl. The term "2H-pyrrolyl" as used herein includes 2H-pyrrol-2-yl, 2H-pyrrol-3-yl, 2H-pyrrol-4-yl and 2H-pyrrol-5-yl. The term "3H-pyrrolyl" as used herein includes 3H-pyrrol-2-yl, 3H-pyrrol-3-yl, 3H-pyrrol-4-yl and 3H-pyrrol-5-yl. The term "dihydrofuranyl" as used herein includes 2,3-dihydrofuran-2-yl, 2,3-dihydrofuran-3-yl, 2,3-dihydrofuran-4-yl, 2,3-dihydrofuran-5-yl, 2,5-dihydrofuran-2-yl, 2,5-dihydrofuran-3-yl, 2,5-dihydrofuran-4-yl and 2,5-dihydrofuran-5-yl. The term "dihydrothiophenyl" as used herein includes 2,3-dihydrothiophen-2-yl, 2,3-dihydrothiophen-3-yl, 2,3-

dihydrothiophen-4-yl, 2,3-dihydrothiophen-5-yl, 2,5-dihydrothiophen-2-yl, 2,5-dihydrothiophen-3-yl, 2,5-dihydrothiophen-4-yl and 2,5-dihydrothiophen-5-yl. The term "imidazolidinyl" as used herein includes imidazolidin-1-yl, imidazolidin-2-yl and imidazolidin-4-yl. The term "pyrazolidinyl" as used herein includes pyrazolidin-1-yl, pyrazolidin-3-yl and pyrazolidin-4-yl. The term "imidazolinyl" as used

5 herein includes imidazolin-1-yl, imidazolin-2-yl, imidazolin-4-yl and imidazolin-5-yl. The term "pyrazolinyl" as used herein includes 1-pyrazolin-3-yl, 1-pyrazolin-4-yl, 2-pyrazolin-1-yl, 2-pyrazolin-3-yl, 2-pyrazolin-4-yl, 2-pyrazolin-5-yl, 3-pyrazolin-1-yl, 3-pyrazolin-2-yl, 3-pyrazolin-3-yl, 3-pyrazolin-4-yl and 3-pyrazolin-5-yl. The term "dioxolanyl" also known as "1,3-dioxolanyl" as used herein includes dioxolan-2-yl, dioxolan-4-yl and dioxolan-5-yl. The term "dioxolyl" also known as "1,3-

10 dioxolyl" as used herein includes dioxol-2-yl, dioxol-4-yl and dioxol-5-yl. The term "oxazolidinyl" as used herein includes oxazolidin-2-yl, oxazolidin-3-yl, oxazolidin-4-yl and oxazolidin-5-yl. The term "isoxazolidinyl" as used herein includes isoxazolidin-2-yl, isoxazolidin-3-yl, isoxazolidin-4-yl and isoxazolidin-5-yl. The term "oxazolinyl" as used herein includes 2-oxazolinyl-2-yl, 2-oxazolinyl-4-yl, 2-oxazolinyl-5-yl, 3-oxazolinyl-2-yl, 3-oxazolinyl-4-yl, 3-oxazolinyl-5-yl, 4-oxazolinyl-2-yl, 4-oxazolinyl-3-

15 yl, 4-oxazolinyl-4-yl and 4-oxazolinyl-5-yl. The term "isoxazolinyl" as used herein includes 2-isoxazolinyl-3-yl, 2-isoxazolinyl-4-yl, 2-isoxazolinyl-5-yl, 3-isoxazolinyl-3-yl, 3-isoxazolinyl-4-yl, 3-isoxazolinyl-5-yl, 4-isoxazolinyl-2-yl, 4-isoxazolinyl-3-yl, 4-isoxazolinyl-4-yl and 4-isoxazolinyl-5-yl. The term "thiazolidinyl" as used herein includes thiazolidin-2-yl, thiazolidin-3-yl, thiazolidin-4-yl and thiazolidin-5-yl. The term "isothiazolidinyl" as used herein includes isothiazolidin-2-yl, isothiazolidin-

20 3-yl, isothiazolidin-4-yl and isothiazolidin-5-yl. The term "chromanyl" as used herein includes chroman-2-yl, chroman-3-yl, chroman-4-yl, chroman-5-yl, chroman-6-yl, chroman-7-yl and chroman-8-yl. The term "thiazolinyl" as used herein includes 2-thiazolinyl-2-yl, 2-thiazolinyl-4-yl, 2-thiazolinyl-5-yl, 3-thiazolinyl-2-yl, 3-thiazolinyl-4-yl, 3-thiazolinyl-5-yl, 4-thiazolinyl-2-yl, 4-thiazolinyl-3-yl, 4-thiazolinyl-4-yl and 4-thiazolinyl-5-yl. The term "isothiazolinyl" as used herein includes 2-

25 isothiazolinyl-3-yl, 2-isothiazolinyl-4-yl, 2-isothiazolinyl-5-yl, 3-isothiazolinyl-3-yl, 3-isothiazolinyl-4-yl, 3-isothiazolinyl-5-yl, 4-isothiazolinyl-2-yl, 4-isothiazolinyl-3-yl, 4-isothiazolinyl-4-yl and 4-isothiazolinyl-5-yl. The term "piperidyl" also known as "piperidinyl" as used herein includes piperid-1-yl, piperid-2-yl, piperid-3-yl and piperid-4-yl. The term "dihydropyridinyl" as used herein includes 1,2-

30 dihydropyridin-1-yl, 1,2-dihydropyridin-2-yl, 1,2-dihydropyridin-3-yl, 1,2-dihydropyridin-4-yl, 1,2-dihydropyridin-5-yl, 1,2-dihydropyridin-6-yl, 1,4-dihydropyridin-1-yl, 1,4-dihydropyridin-2-yl, 1,4-dihydropyridin-3-yl, 1,4-dihydropyridin-4-yl, 2,3-dihydropyridin-2-yl, 2,3-dihydropyridin-3-yl, 2,3-dihydropyridin-4-yl, 2,3-dihydropyridin-5-yl, 2,3-dihydropyridin-6-yl, 2,5-dihydropyridin-2-yl, 2,5-dihydropyridin-3-yl, 2,5-dihydropyridin-4-yl, 2,5-dihydropyridin-5-yl, 2,5-dihydropyridin-6-yl, 3,4-

35 dihydropyridin-2-yl, 3,4-dihydropyridin-3-yl, 3,4-dihydropyridin-4-yl, 3,4-dihydropyridin-5-yl and 3,4-dihydropyridin-6-yl. The term "tetrahydropyridinyl" as used herein includes 1,2,3,4-tetrahydropyridin-1-yl, 1,2,3,4-tetrahydropyridin-2-yl, 1,2,3,4-tetrahydropyridin-3-yl, 1,2,3,4-tetrahydropyridin-4-yl, 1,2,3,4-tetrahydropyridin-5-yl, 1,2,3,4-tetrahydropyridin-6-yl, 1,2,3,6-tetrahydropyridin-1-yl, 1,2,3,6-tetrahydropyridin-2-yl, 1,2,3,6-tetrahydropyridin-3-yl, 1,2,3,6-tetrahydropyridin-4-yl, 1,2,3,6-tetrahydropyridin-5-yl, 1,2,3,6-tetrahydropyridin-6-yl, 2,3,4,5-tetrahydropyridin-2-yl, 2,3,4,5-

tetrahydropyridin-3-yl, 2,3,4,5-tetrahydropyridin-3-yl, 2,3,4,5-tetrahydropyridin-4-yl, 2,3,4,5-tetrahydropyridin-5-yl and 2,3,4,5-tetrahydropyridin-6-yl. The term "tetrahydropyranyl" also known as "oxanyl" or "tetrahydro-2H-pyranyl", as used herein includes tetrahydropyran-2-yl, tetrahydropyran-3-yl and tetrahydropyran-4-yl. The term "2H-pyranyl" as used herein includes 2H-pyran-2-yl, 2H-pyran-3-yl, 2H-pyran-4-yl, 2H-pyran-5-yl and 2H-pyran-6-yl. The term "4H-pyranyl" as used herein includes 4H-pyran-2-yl, 4H-pyran-3-yl and 4H-pyran-4-yl. The term "3,4-dihydro-2H-pyranyl" as used herein includes 3,4-dihydro-2H-pyran-2-yl, 3,4-dihydro-2H-pyran-3-yl, 3,4-dihydro-2H-pyran-4-yl, 3,4-dihydro-2H-pyran-5-yl and 3,4-dihydro-2H-pyran-6-yl. The term "3,6-dihydro-2H-pyranyl" as used herein includes 3,6-dihydro-2H-pyran-2-yl, 3,6-dihydro-2H-pyran-3-yl, 3,6-dihydro-2H-pyran-4-yl, 3,6-dihydro-2H-pyran-5-yl and 3,6-dihydro-2H-pyran-6-yl. The term "tetrahydrothiophenyl", as used herein includes tetrahydrothiophen-2-yl, tetrahydrothiophenyl -3-yl and tetrahydrothiophenyl -4-yl. The term "2H-thiopyranyl" as used herein includes 2H-thiopyran-2-yl, 2H-thiopyran-3-yl, 2H-thiopyran-4-yl, 2H-thiopyran-5-yl and 2H-thiopyran-6-yl. The term "4H-thiopyranyl" as used herein includes 4H-thiopyran-2-yl, 4H-thiopyran-3-yl and 4H-thiopyran-4-yl. The term "3,4-dihydro-2H-thiopyranyl" as used herein includes 3,4-dihydro-2H-thiopyran-2-yl, 3,4-dihydro-2H-thiopyran-3-yl, 3,4-dihydro-2H-thiopyran-4-yl, 3,4-dihydro-2H-thiopyran-5-yl and 3,4-dihydro-2H-thiopyran-6-yl. The term "3,6-dihydro-2H-thiopyranyl" as used herein includes 3,6-dihydro-2H-thiopyran-2-yl, 3,6-dihydro-2H-thiopyran-3-yl, 3,6-dihydro-2H-thiopyran-4-yl, 3,6-dihydro-2H-thiopyran-5-yl and 3,6-dihydro-2H-thiopyran-6-yl. The term "piperaziny" also known as "piperazidiny" as used herein includes piperazin-1-yl and piperazin-2-yl. The term "morpholinyl" as used herein includes morpholin-2-yl, morpholin-3-yl and morpholin-4-yl. The term "thiomorpholinyl" as used herein includes thiomorpholin-2-yl, thiomorpholin-3-yl and thiomorpholin-4-yl. The term "dioxanyl" as used herein includes 1,2-dioxan-3-yl, 1,2-dioxan-4-yl, 1,3-dioxan-2-yl, 1,3-dioxan-4-yl, 1,3-dioxan-5-yl and 1,4-dioxan-2-yl. The term "dithianyl" as used herein includes 1,2-dithian-3-yl, 1,2-dithian-4-yl, 1,3-dithian-2-yl, 1,3-dithian-4-yl, 1,3-dithian-5-yl and 1,4-dithian-2-yl. The term "oxathianyl" as used herein includes oxathian-2-yl and oxathian-3-yl. The term "trioxanyl" as used herein includes 1,2,3-trioxan-4-yl, 1,2,3-trioxan-5-yl, 1,2,4-trioxan-3-yl, 1,2,4-trioxan-5-yl, 1,2,4-trioxan-6-yl and 1,3,4-trioxan-2-yl. The term "azepanyl" as used herein includes azepan-1-yl, azepan-2-yl, azepan-3-yl and azepan-4-yl. The term "homopiperaziny" as used herein includes homopiperazin-1-yl, homopiperazin-2-yl, homopiperazin-3-yl and homopiperazin-4-yl. The term "indolinyl" as used herein includes indolin-1-yl, indolin-2-yl, indolin-3-yl, indolin-4-yl, indolin-5-yl, indolin-6-yl, and indolin-7-yl. The term "quinoliziny" as used herein includes quinolizidin-1-yl, quinolizidin-2-yl, quinolizidin-3-yl and quinolizidin-4-yl. The term "isoindolinyl" as used herein includes isoindolin-1-yl, isoindolin-2-yl, isoindolin-3-yl, isoindolin-4-yl, isoindolin-5-yl, isoindolin-6-yl, and isoindolin-7-yl. The term "3H-indolyl" as used herein includes 3H-indol-2-yl, 3H-indol-3-yl, 3H-indol-4-yl, 3H-indol-5-yl, 3H-indol-6-yl, and 3H-indol-7-yl. The term "quinoliziny" as used herein includes quinolizidin-1-yl, quinolizidin-2-yl, quinolizidin-3-yl and quinolizidin-4-yl. The term "quinoliziny" as used herein includes quinolizidin-1-yl, quinolizidin-2-yl, quinolizidin-3-yl and quinolizidin-4-yl. The term "tetrahydroquinolinyl" as used herein includes tetrahydroquinolin-1-yl, tetrahydroquinolin-2-yl, tetrahydroquinolin-3-yl,

tetrahydroquinolin-4-yl, tetrahydroquinolin-5-yl, tetrahydroquinolin-6-yl, tetrahydroquinolin-7-yl and tetrahydroquinolin-8-yl. The term "tetrahydroisoquinolinyl" as used herein includes tetrahydroisoquinolin-1-yl, tetrahydroisoquinolin-2-yl, tetrahydroisoquinolin-3-yl, tetrahydroisoquinolin-4-yl, tetrahydroisoquinolin-5-yl, tetrahydroisoquinolin-6-yl, 5 tetrahydroisoquinolin-7-yl and tetrahydroisoquinolin-8-yl. The term "1H-pyrrolizine" as used herein includes 1H-pyrrolizin-1-yl, 1H-pyrrolizin-2-yl, 1H-pyrrolizin-3-yl, 1H-pyrrolizin-5-yl, 1H-pyrrolizin-6-yl and 1H-pyrrolizin-7-yl. The term "3H-pyrrolizine" as used herein includes 3H-pyrrolizin-1-yl, 3H-pyrrolizin-2-yl, 3H-pyrrolizin-3-yl, 3H-pyrrolizin-5-yl, 3H-pyrrolizin-6-yl and 3H-pyrrolizin-7-yl.

When the suffix "ene" is used in conjunction with a heterocyclyl group, i.e. "heterocyclylene", this is 10 intended to mean the heterocyclyl group as defined herein having two single bonds as points of attachment to other groups.

The term "heterocyclalkyl", as a group or part of a group, means an alkyl as defined herein, wherein at least one hydrogen atom is replaced by at least one heterocyclyl as defined herein.

The term "heteroaryl" as a group or part of a group, refers but is not limited to 5 to 12 atom aromatic 15 rings or ring systems containing 1 or 2 rings which can be fused together or linked covalently, typically containing 5 to 6 atoms; at least one of which is aromatic in which one or more carbon atoms in one or more of these rings can be replaced by N, O and/or S atoms where the N and S heteroatoms may optionally be oxidized and the N heteroatoms may optionally be quaternized, and wherein at least one carbon atom of said heteroaryl can be oxidized to form at least one C=O. Such 20 rings may be fused to an aryl, cycloalkyl, heteroaryl or heterocyclyl ring. Non-limiting examples of such heteroaryl, include: pyrrolyl, furanyl, thiophenyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, oxatriazolyl, thiatriazolyl, pyridinyl, pyrimidyl, pyrazinyl, pyridazinyl, oxazinyl, dioxinyl, thiazinyl, triazinyl, imidazo[2,1-b][1,3]thiazolyl, thieno[3,2-b]furanyl, thieno[3,2-b]thiophenyl, thieno[2,3-d][1,3]thiazolyl, thieno[2,3-d]imidazolyl, 25 tetrazolo[1,5-a]pyridinyl, indolyl, indoliziny, isoindolyl, benzofuranyl, isobenzofuranyl, benzothiophenyl, isobenzothiophenyl, indazolyl, benzimidazolyl, 1,3-benzoxazolyl, 1,2-benzisoxazolyl, 2,1-benzisoxazolyl, 1,3-benzothiazolyl, 1,2-benzoisothiazolyl, 2,1-benzoisothiazolyl, benzotriazolyl, 1,2,3-benzoxadiazolyl, 2,1,3-benzoxadiazolyl, 1,2,3-benzothiadiadiazolyl, 2,1,3-benzothiadiadiazolyl, benzo[d]oxazol-2(3H)-one, 2,3-dihydro-benzofuranyl, thienopyridinyl, purinyl, 30 imidazo[1,2-a]pyridinyl, 6-oxo-pyridazin-1(6H)-yl, 2-oxopyridin-1(2H)-yl, 6-oxo-pyridazin-1(6H)-yl, 2-oxopyridin-1(2H)-yl, 1,3-benzodioxolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, quinoxalinyl; preferably said heteroaryl group is selected from the group consisting of pyridyl, 1,3-benzodioxolyl, benzo[d]oxazol-2(3H)-one, 2,3-dihydro-benzofuranyl, pyrazinyl, pyrazolyl, pyrrolyl, isoxazolyl, thiophenyl, imidazolyl, benzimidazolyl, pyrimidinyl, triazolyl and thiazolyl.

35 The term "pyrrolyl" (also called azolyl) as used herein includes pyrrol-1-yl, pyrrol-2-yl and pyrrol-3-yl. The term "furanyl" (also called "furyl") as used herein includes furan-2-yl and furan-3-yl (also called furan-2-yl and furan-3-yl). The term "thiophenyl" (also called "thienyl") as used herein includes thiophen-2-yl and thiophen-3-yl (also called thien-2-yl and thien-3-yl). The term "pyrazolyl" (also

called 1H-pyrazolyl and 1,2-diazolyl) as used herein includes pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl and pyrazol-5-yl. The term "imidazolyl" as used herein includes imidazol-1-yl, imidazol-2-yl, imidazol-4-yl and imidazol-5-yl. The term "oxazolyl" (also called 1,3-oxazolyl) as used herein includes oxazol-2-yl, oxazol-4-yl and oxazol-5-yl. The term "isoxazolyl" (also called 1,2-oxazolyl), as used herein includes isoxazol-3-yl, isoxazol-4-yl, and isoxazol-5-yl. The term "thiazolyl" (also called 1,3-thiazolyl), as used herein includes thiazol-2-yl, thiazol-4-yl and thiazol-5-yl (also called 2-thiazolyl, 4-thiazolyl and 5-thiazolyl). The term "isothiazolyl" (also called 1,2-thiazolyl) as used herein includes isothiazol-3-yl, isothiazol-4-yl, and isothiazol-5-yl. The term "triazolyl" as used herein includes 1H-triazolyl and 4H-1,2,4-triazolyl, "1H-triazolyl" includes 1H-1,2,3-triazol-1-yl, 1H-1,2,3-triazol-4-yl, 1H-1,2,3-triazol-5-yl, 1H-1,2,4-triazol-1-yl, 1H-1,2,4-triazol-3-yl and 1H-1,2,4-triazol-5-yl. "4H-1,2,4-triazolyl" includes 4H-1,2,4-triazol-4-yl, and 4H-1,2,4-triazol-3-yl. The term "oxadiazolyl" as used herein includes 1,2,3-oxadiazol-4-yl, 1,2,3-oxadiazol-5-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, 1,2,5-oxadiazol-3-yl and 1,3,4-oxadiazol-2-yl. The term "thiadiazolyl" as used herein includes 1,2,3-thiadiazol-4-yl, 1,2,3-thiadiazol-5-yl, 1,2,4-thiadiazol-3-yl, 1,2,4-thiadiazol-5-yl, 1,2,5-thiadiazol-3-yl (also called furazan-3-yl) and 1,3,4-thiadiazol-2-yl. The term "tetrazolyl" as used herein includes 1H-tetrazol-1-yl, 1H-tetrazol-5-yl, 2H-tetrazol-2-yl, and 2H-tetrazol-5-yl. The term "oxatriazolyl" as used herein includes 1,2,3,4-oxatriazol-5-yl and 1,2,3,5-oxatriazol-4-yl. The term "thiatriazolyl" as used herein includes 1,2,3,4-thiatriazol-5-yl and 1,2,3,5-thiatriazol-4-yl. The term "pyridinyl" (also called "pyridyl") as used herein includes pyridin-2-yl, pyridin-3-yl and pyridin-4-yl (also called 2-pyridyl, 3-pyridyl and 4-pyridyl). The term "pyrimidyl" as used herein includes pyrimid-2-yl, pyrimid-4-yl, pyrimid-5-yl and pyrimid-6-yl. The term "pyrazinyl" as used herein includes pyrazin-2-yl and pyrazin-3-yl. The term "pyridazinyl" as used herein includes pyridazin-3-yl and pyridazin-4-yl. The term "oxazinyl" (also called "1,4-oxazinyl") as used herein includes 1,4-oxazin-4-yl and 1,4-oxazin-5-yl. The term "dioxinyl" (also called "1,4-dioxinyl") as used herein includes 1,4-dioxin-2-yl and 1,4-dioxin-3-yl. The term "thiazinyl" (also called "1,4-thiazinyl") as used herein includes 1,4-thiazin-2-yl, 1,4-thiazin-3-yl, 1,4-thiazin-4-yl, 1,4-thiazin-5-yl and 1,4-thiazin-6-yl. The term "triazinyl" as used herein includes 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-5-yl, 1,2,4-triazin-6-yl, 1,2,3-triazin-4-yl and 1,2,3-triazin-5-yl. The term "imidazo[2,1-b][1,3]thiazolyl" as used herein includes imidazo[2,1-b][1,3]thiazol-2-yl, imidazo[2,1-b][1,3]thiazol-3-yl, imidazo[2,1-b][1,3]thiazol-5-yl and imidazo[2,1-b][1,3]thiazol-6-yl. The term "thieno[3,2-b]furanyl" as used herein includes thieno[3,2-b]furan-2-yl, thieno[3,2-b]furan-3-yl, thieno[3,2-b]furan-4-yl, and thieno[3,2-b]furan-5-yl. The term "thieno[3,2-b]thiophenyl" as used herein includes thieno[3,2-b]thien-2-yl, thieno[3,2-b]thien-3-yl, thieno[3,2-b]thien-5-yl and thieno[3,2-b]thien-6-yl. The term "thieno[2,3-d][1,3]thiazolyl" as used herein includes thieno[2,3-d][1,3]thiazol-2-yl, thieno[2,3-d][1,3]thiazol-5-yl and thieno[2,3-d][1,3]thiazol-6-yl. The term "thieno[2,3-d]imidazolyl" as used herein includes thieno[2,3-d]imidazol-2-yl, thieno[2,3-d]imidazol-4-yl and thieno[2,3-d]imidazol-5-yl. The term "tetrazolo[1,5-a]pyridinyl" as used herein includes tetrazolo[1,5-a]pyridine-5-yl, tetrazolo[1,5-a]pyridine-6-yl, tetrazolo[1,5-a]pyridine-7-yl, and tetrazolo[1,5-a]pyridine-8-yl. The term "indolyl" as used herein includes indol-1-yl, indol-2-yl, indol-3-yl, indol-4-yl, indol-5-yl, indol-6-yl and indol-7-yl. The term "indoliziny" as used herein includes

indolizin-1-yl, indolizin-2-yl, indolizin-3-yl, indolizin-5-yl, indolizin-6-yl, indolizin-7-yl, and indolizin-8-yl. The term "isoindolyl" as used herein includes isoindol-1-yl, isoindol-2-yl, isoindol-3-yl, isoindol-4-yl, isoindol-5-yl, isoindol-6-yl and isoindol-7-yl. The term "benzofuranyl" (also called benzo[b]furanyl) as used herein includes benzofuran-2-yl, benzofuran-3-yl, benzofuran-4-yl, benzofuran-5-yl, 5 benzofuran-6-yl and benzofuran-7-yl. The term "isobenzofuranyl" (also called benzo[c]furanyl) as used herein includes isobenzofuran-1-yl, isobenzofuran-3-yl, isobenzofuran-4-yl, isobenzofuran-5-yl, isobenzofuran-6-yl and isobenzofuran-7-yl. The term "benzothiophenyl" (also called benzo[b]thienyl) as used herein includes 2-benzo[b]thiophenyl, 3-benzo[b]thiophenyl, 4-benzo[b]thiophenyl, 5-benzo[b]thiophenyl, 6-benzo[b]thiophenyl and -7-benzo[b]thiophenyl (also called benzothien-2-yl, 10 benzothien-3-yl, benzothien-4-yl, benzothien-5-yl, benzothien-6-yl and benzothien-7-yl). The term "isobenzothiophenyl" (also called benzo[c]thienyl) as used herein includes isobenzothien-1-yl, isobenzothien-3-yl, isobenzothien-4-yl, isobenzothien-5-yl, isobenzothien-6-yl and isobenzothien-7-yl. The term "indazolyl" (also called 1H-indazolyl or 2-azaindolyl) as used herein includes 1H-indazol-1-yl, 1H-indazol-3-yl, 1H-indazol-4-yl, 1H-indazol-5-yl, 1H-indazol-6-yl, 1H-indazol-7-yl, 2H-indazol-15 2-yl, 2H-indazol-3-yl, 2H-indazol-4-yl, 2H-indazol-5-yl, 2H-indazol-6-yl, and 2H-indazol-7-yl. The term "benzimidazolyl" as used herein includes benzimidazol-1-yl, benzimidazol-2-yl, benzimidazol-4-yl, benzimidazol-5-yl, benzimidazol-6-yl and benzimidazol-7-yl. The term "1,3-benzoxazolyl" as used herein includes 1,3-benzoxazol-2-yl, 1,3-benzoxazol-4-yl, 1,3-benzoxazol-5-yl, 1,3-benzoxazol-6-yl and 1,3-benzoxazol-7-yl. The term "1,2-benzisoxazolyl" as used herein includes 1,2-benzisoxazol-3-yl, 1,2-benzisoxazol-4-yl, 1,2-benzisoxazol-5-yl, 1,2-benzisoxazol-6-yl and 1,2-benzisoxazol-7-yl. 20 The term "2,1-benzisoxazolyl" as used herein includes 2,1-benzisoxazol-3-yl, 2,1-benzisoxazol-4-yl, 2,1-benzisoxazol-5-yl, 2,1-benzisoxazol-6-yl and 2,1-benzisoxazol-7-yl. The term "1,3-benzothiazolyl" as used herein includes 1,3-benzothiazol-2-yl, 1,3-benzothiazol-4-yl, 1,3-benzothiazol-5-yl, 1,3-benzothiazol-6-yl and 1,3-benzothiazol-7-yl. The term "1,2-benzisothiazolyl" as used herein includes 1,2-benzisothiazol-3-yl, 1,2-benzisothiazol-4-yl, 1,2-benzisothiazol-5-yl, 1,2-benzisothiazol-6-yl and 1,2-benzisothiazol-7-yl. 25 The term "2,1-benzisothiazolyl" as used herein includes 2,1-benzisothiazol-3-yl, 2,1-benzisothiazol-4-yl, 2,1-benzisothiazol-5-yl, 2,1-benzisothiazol-6-yl and 2,1-benzisothiazol-7-yl. The term "benzotriazolyl" as used herein includes benzotriazol-1-yl, benzotriazol-4-yl, benzotriazol-5-yl, benzotriazol-6-yl and benzotriazol-7-yl. The term "1,2,3-benzoxadiazolyl" as used herein includes 1,2,3-benzoxadiazol-4-yl, 1,2,3-benzoxadiazol-5-yl, 1,2,3-benzoxadiazol-6-yl and 1,2,3-benzoxadiazol-7-yl. The term "2,1,3-benzoxadiazolyl" as used herein includes 2,1,3-benzoxadiazol-4-yl, 2,1,3-benzoxadiazol-5-yl, 2,1,3-benzoxadiazol-6-yl and 2,1,3-benzoxadiazol-7-yl. The term "1,2,3-benzothiadiazolyl" as used herein includes 1,2,3-benzothiadiazol-4-yl, 1,2,3-benzothiadiazol-5-yl, 1,2,3-benzothiadiazol-6-yl and 1,2,3-benzothiadiazol-7-yl. 30 benzothiadiazol-7-yl. The term "2,1,3-benzothiadiazolyl" as used herein includes 2,1,3-benzothiadiazol-4-yl, 2,1,3-benzothiadiazol-5-yl, 2,1,3-benzothiadiazol-6-yl and 2,1,3-benzothiadiazol-7-yl. The term "thienopyridinyl" as used herein includes thieno[2,3-b]pyridinyl, thieno[2,3-c]pyridinyl, thieno[3,2-c]pyridinyl and thieno[3,2-b]pyridinyl. The term "purinyl" as used herein includes purin-2-yl, purin-6-yl, purin-7-yl and purin-8-yl. The term "imidazo[1,2-a]pyridinyl", as

used herein includes imidazo[1,2-a]pyridin-2-yl, imidazo[1,2-a]pyridin-3-yl, imidazo[1,2-a]pyridin-4-yl, imidazo[1,2-a]pyridin-5-yl, imidazo[1,2-a]pyridin-6-yl and imidazo[1,2-a]pyridin-7-yl. The term "1,3-benzodioxolyl", as used herein includes 1,3-benzodioxol-4-yl, 1,3-benzodioxol-5-yl, 1,3-benzodioxol-6-yl, and 1,3-benzodioxol-7-yl. The term "quinolinyl" as used herein includes quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, quinolin-5-yl, quinolin-6-yl, quinolin-7-yl and quinolin-8-yl. The term "isoquinolinyl" as used herein includes isoquinolin-1-yl, isoquinolin-3-yl, isoquinolin-4-yl, isoquinolin-5-yl, isoquinolin-6-yl, isoquinolin-7-yl and isoquinolin-8-yl. The term "cinnolinyl" as used herein includes cinnolin-3-yl, cinnolin-4-yl, cinnolin-5-yl, cinnolin-6-yl, cinnolin-7-yl and cinnolin-8-yl. The term "quinazolinyl" as used herein includes quinazolin-2-yl, quinazolin-4-yl, quinazolin-5-yl, quinazolin-6-yl, quinazolin-7-yl and quinazolin-8-yl. The term "quinoxaliny" as used herein includes quinoxalin-2-yl, quinoxalin-5-yl, and quinoxalin-6-yl.

When the suffix "ene" is used in conjunction with a heteroaryl group, i.e. "heteroarylene", this is intended to mean the heteroaryl group as defined herein having two single bonds as points of attachment to other groups.

The term "heteroarylalkyl", as a group or part of a group, means an alkyl as defined herein, wherein at least one hydrogen atom is replaced by at least one heteroaryl as defined herein.

The term "mono- or di-alkylamino", as a group or part of a group, refers to a group of formula $-N(R^o)(R^p)$ wherein R^o and R^p are each independently selected from hydrogen, or C_{1-6} alkyl, wherein at least one of R^o or R^p is C_{1-6} alkyl. Thus, alkylamino include mono-alkyl amino group (e.g. mono- C_{1-6} alkylamino group such as methylamino and ethylamino), and di-alkylamino group (e.g. di-alkylamino group such as dimethylamino and diethylamino). Non-limiting examples of suitable mono- or di- C_{1-6} alkylamino groups include *n*-propylamino, isopropylamino, *n*-butylamino, *i*-butylamino, *sec*-butylamino, *t*-butylamino, pentylamino, *n*-hexylamino, di-*n*-propylamino, di-*i*-propylamino, ethylmethylamino, methyl-*n*-propylamino, methyl-*i*-propylamino, *n*-butylmethylamino, *i*-butylmethylamino, *t*-butylmethylamino, ethyl-*n*-propylamino, ethyl-*i*-propylamino, *n*-butylethylamino, *i*-butylethylamino, *t*-butylethylamino, di-*n*-butylamino, di-*i*-butylamino, methylpentylamino, methylhexylamino, ethylpentylamino, ethylhexylamino, propylpentylamino, propylhexylamino, and the like.

The term "mono- or di-arylamino", as a group or part of a group, refers to a group of formula $-N(R^q)(R^r)$ wherein R^q and R^r are each independently selected from hydrogen, aryl, or alkyl, wherein at least one of R^q or R^r is C_{6-12} aryl.

The term "mono- or di-cycloalkylamino", as a group or part of a group, refers to a group of formula $-N(R^s)(R^t)$ wherein R^s and R^t are each independently selected from hydrogen, cycloalkyl, or alkyl, wherein at least one of R^s or R^t is cycloalkyl.

The term "aminoalkyl", as a group or part of a group, refers to a group of formula $-R^a-NR^oR^p$ wherein R^a is C_{1-6} alkylene, R^o is hydrogen or alkyl as defined herein, and R^p is hydrogen or C_{1-6} alkyl as defined herein.

The term “mono- or di-heteroaryl-amino”, as a group or part of a group, refers to a group of formula $-N(R^U)(R^V)$ wherein R^U and R^V are each independently selected from hydrogen, heteroaryl, or C_{1-6} alkyl, wherein at least one of R^U or R^V is heteroaryl as defined herein.

The term “mono- or di-heterocyclylamino”, as a group or part of a group, refers to a group of formula $-N(R^W)(R^X)$ wherein R^W and R^X are each independently selected from hydrogen, heterocyclyl, or C_{1-6} alkyl, wherein at least one of R^W or R^X is heterocyclyl as defined herein.

The term “hydroxycarbonylalkyl”, as a group or part of a group, refers to a group of formula $-R^a-COOH$, wherein R^a is alkylene as defined herein.

The term “alkyloxycarbonyl”, as a group or part of a group, refers to a group of formula $-COO-R^b$, wherein R^b is alkyl as defined herein.

The term “mono- or dialkylaminocarbonyl”, as a group or part of a group, refers to a group of formula $-CONR^OR^P$ wherein R^OR^P are each independently selected from hydrogen, or C_{1-6} alkyl, wherein at least one of R^O or R^P is C_{1-6} alkyl.

The term “alkylcarbonyl”, as a group or part of a group, refers to a group of formula $-CO-R^b$, wherein R^b is alkyl as defined herein.

The term “alkylcarbonylamino”, as a group or part of a group, refers to a group of formula $-NR^O-CO-R^b$, wherein R^O is selected from hydrogen, or alkyl and R^b is alkyl as defined herein.

The term “mono or di-alkylaminocarbonyl C_{1-6} alkyl”, as a group or part of a group, refers to a group of formula $-R^a-CONR^OR^P$ wherein R^OR^P are each independently selected from hydrogen, or alkyl, wherein at least one of R^O or R^P is alkyl, and R^a is alkylene as defined herein.

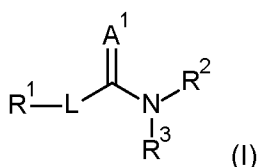
The term “leaving group” as used herein means a chemical group which is susceptible to be displaced by a nucleophile or cleaved off or hydrolyzed in basic or acidic conditions. In a particular embodiment, a leaving group is selected from a halogen atom (e.g., Cl, Br, I) or a trihalomethyl group (e.g. CCl_3 , Cl_3 , CBr_3).

The term “a saturated or unsaturated 3-, 4-, 5-, 6- or 7-membered ring” as used herein encompasses saturated or unsaturated carbon only membered rings, as well as saturated or unsaturated heteroatoms containing rings. The term “a saturated 3-, 4-, 5-, 6- or 7- carbon membered ring” as used herein refers to saturated carbon only membered ring such as C_3 - $_7$ cycloalkyl and C_{3-7} cycloalkylene.

Whenever used in the present invention the term “compounds of the invention” or a similar term is meant to include the compounds of general formula (I) and any subgroup thereof. This term also refers to the compounds as depicted in Table 1 and their derivatives, N-oxides, salts, solvates, hydrates, stereoisomeric forms, racemic mixtures, tautomeric forms, optical isomers, analogues, prodrugs, esters and metabolites, as well as their quaternized nitrogen analogues. The N-oxide forms of said compounds are meant to comprise compounds wherein one or several nitrogen atoms are oxidized to the so-called N-oxide.

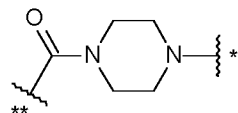
Preferred statements, features, and embodiments of the compounds, methods and uses of this invention are set herein below. Each statements and embodiments of the invention so defined may be combined with any other statement and/or embodiments unless clearly indicated to the contrary. In particular, any feature indicated as being preferred or advantageous may be combined with any other feature or features or statements indicated as being preferred or advantageous. Hereto, the present invention is in particular captured by any one or any combination of one or more of the below numbered aspects and embodiments 1 to 86, with any other statement and/or embodiments.

1. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof,



wherein,

A^1 is selected from the group consisting of S; and O;

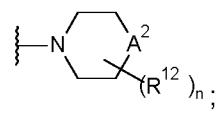
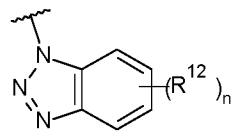
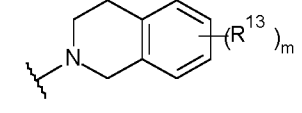
L is selected from the group consisting of $\text{C}=\text{O}$; S; NR^5 ; $^*\text{NR}^6-\text{NR}^7-\text{C}(\text{O})^{**}$; ; $\text{C}=\text{S}$; and a single bond; wherein * represents where L is bound to $\text{C}=\text{A}^1$; and ** represents where L is bound to R^1 ; and wherein,

R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from

the group consisting of ; ; ; wherein,

A^2 is selected from the group consisting of O; NR^9 ; NH; $\text{CR}^{10}\text{R}^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

R¹⁰ is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be unsubstituted or substituted with one or more Z⁵;

R¹¹ is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be unsubstituted or substituted with one or more Z⁶;

each R¹² is independently selected from the group consisting of hydrogen; halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two R¹² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹³ is independently selected from the group consisting of hydrogen; halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two R¹³ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

R⁵ is selected from the group consisting of hydrogen, alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

5 each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

10 each R^{17} is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

15 or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R^{18} is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; 20 wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{19} is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at 25 least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and 30 heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroarylheterocyclyl, heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; 35 carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z^2 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^2 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at

least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl or aryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl or arylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH or S;

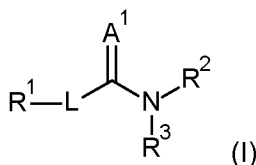
and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁹, O or S; R¹ is aryl; then L is not S;

and with the proviso that said compound is not

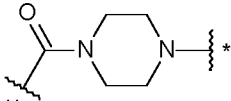
- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(4-phenylphenyl)-2-thioxo-ethanone;
- 4-benzyl-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carbothioamide;
- (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-(4-fluorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-nitrophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-bromophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 1-morpholino-2-phenyl-ethanethione;

- N-phenylmorpholine-4-carboxamide;
 - (4-phenylphenyl)-(4-phenylpiperazin-1-yl)methanethione;
 - 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
 - 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
 - 5 - 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
 - 2-(4-methyl-1-piperidyl)-1-phenyl-2-thioxo-ethanone;
 - 4-(2-morpholino-2-thioxo-acetyl)benzoic acid;
 - 1-morpholino-2-phenyl-ethane-1,2-dione;
 - 2-hydroxy-1-morpholino-2-phenyl-ethanone;
 - 10 - N-morpholinobenzamide;
 - 1-morpholino-3-phenyl-urea.
2. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof,



15 wherein,

A¹ is selected from the group consisting of S; and O;

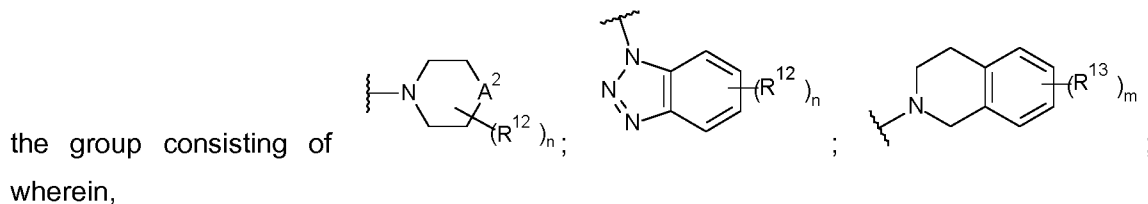
L is selected from the group consisting of C=O; S; NR⁵; *NR⁶-NR⁷-C(O)**; ; C=S; and a single bond; wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹; and wherein,

20 R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

25 R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z³;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from



A^2 is selected from the group consisting of O; NR^9 ; NH; $CR^{10}R^{11}$; and S;

5 n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;

carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

R^5 is selected from the group consisting of hydrogen, alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{17} is independently selected from the group consisting of hydrogen; $-\text{NH}_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;

each R^{18} is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{19} is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl,

cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroaryheterocyclyl, heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z³ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at

least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl or aryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl or arylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH or S;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

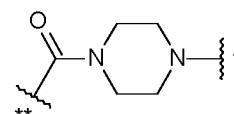
and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁹, O or S; R¹ is aryl; then L is not S;

and with the proviso that said compound is not

- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(4-phenylphenyl)-2-thioxo-ethanone;
- 4-benzyl-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carbothioamide;
- (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;

- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-(4-fluorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 5 - 1-(4-nitrophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-bromophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 1-morpholino-2-phenyl-ethanethione;
- N-phenylmorpholine-4-carboxamide;
- 10 - (4-phenylphenyl)-(4-phenylpiperazin-1-yl)methanethione;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-(4-methyl-1-piperidyl)-1-phenyl-2-thioxo-ethanone;
- 15 - 4-(2-morpholino-2-thioxo-acetyl)benzoic acid;
- 1-morpholino-2-phenyl-ethane-1,2-dione;
- 2-hydroxy-1-morpholino-2-phenyl-ethanone;
- N-morpholinobenzamide;
- 1-morpholino-3-phenyl-urea;
- 20 - 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(p-tolyl)-2-thioxo-ethanone;
- 2-(4-ethylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-cyclohexyl-2-oxo-2-phenyl-thioacetamide;
- 25 - 1-(3-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-ethoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 2-morpholino-1-(2-naphthyl)-2-thioxo-ethanone;
- 2-morpholino-1-(1-naphthyl)-2-thioxo-ethanone;
- 1-(2-furyl)-2-morpholino-2-thioxo-ethanone;
- 30 - 2-morpholino-1-(2-thienyl)-2-thioxo-ethanone;
- 1-(benzofuran-2-yl)-2-morpholino-2-thioxo-ethanone;
- 2-oxo-2-phenyl-N-(p-tolyl)thioacetamide;
- 2-oxo-N,2-diphenyl-thioacetamide;
- N-(4-fluorophenyl)-2-oxo-2-phenyl-thioacetamide;
- 35 - N-(4-chlorophenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-bromophenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-isopropylphenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-methoxyphenyl)-2-oxo-2-phenyl-thioacetamide;
- 2-oxo-N-phenyl-2-(p-tolyl)thioacetamide;

- N-[3-[2-(1-piperidyl)-2-thioxo-acetyl]phenyl]acetamide;
 - 1-(5-chloro-2-phenoxy-phenyl)-2-morpholino-2-thioxo-ethanone;
 - 1-[2-(4-chlorophenoxy)phenyl]-2-morpholino-2-thioxo-ethanone;
 - methyl 4-(2-morpholino-2-thioxo-acetyl)benzoate;
 - 5 - 1-(2-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
 - 2-(2-chlorophenyl)-N,N-dimethyl-2-oxo-thioacetamide;
 - 2-(4-chlorophenyl)-N,N-dimethyl-2-oxo-thioacetamide;
 - N,N-dimethyl-2-(1-naphthyl)-2-oxo-thioacetamide;
 - N-benzyl-N-methyl-2-oxo-2-phenyl-thioacetamide;
 - 10 - 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
 - N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;
 - N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
 - N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;
 - N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-
 - 15 carbothioamide.
3. The compound according to any one of statements 1 or 2, wherein "alkyl" as a group or part of a group is C₁₋₆alkyl, "alkenyl" as a group or part of a group is C₂₋₆alkenyl, "alkynyl" as a group or part of a group, is C₂₋₆alkynyl, "cycloalkyl", as a group or part of a group, is C₃₋₁₂cycloalkyl, "aryl", as a group or part of a group, is C₆₋₁₂aryl.
- 20 4. The compound according to any one of statements 1 to 3, wherein A¹ is S.
5. The compound according to any one of statements 1 to 3, wherein A¹ is O.
6. The compound according to any one of statements 1 to 5, wherein L is C=O.
7. The compound according to any one of statements 1 to 6, wherein L is S.
8. The compound according to any one of statements 1 to 7, wherein L is NR⁵ and R⁵ is selected
- 25 from the group consisting of hydrogen, alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl.
9. The compound according to any one of statements 1 to 8, wherein L is *NR⁶-NR⁷-C(O)**,
- wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹, R⁶ is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl;
- 30 heteroaryl; heterocyclalkyl; and heteroarylalkyl; R⁷ is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl.



10. The compound according to any one of statements 1 to 5, wherein L is
- wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹.
- 35 11. The compound according to any one of statements 1 to 5, wherein L is C=S.
12. The compound according to any one of statements 1 to 5, wherein L is a single bond.

13. The compound according to any one of statements 1 to 12, wherein R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; haloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 , preferably R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; arylalkyl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 , preferably R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 , preferably R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; alkyl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 , for example one, two or three Z^1 .

14. The compound according to any one of statements 1 to 13, wherein each Z^1 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroaryheterocyclyl, heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$, preferably each Z^1 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroaryheterocyclyl, heterocyclyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$, preferably each Z^1 is independently selected from the group consisting of halo; $-NO_2$; aryl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; heteroaryl; heteroaryheterocyclyl, $-NR^{16}R^{17}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-NHC(O)R^{20}$; and $-NHC(O)NR^{16}R^{17}$,

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

each R^{17} is independently selected from the group consisting of hydrogen; $-NH_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;

each R^{18} is independently selected from the group consisting of alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one

carbon atom or heteroatom of said alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S.

15. The compound according to any one of statements 1 to 14, wherein R² is selected from the group consisting of arylalkyl; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²,

16. The compound according to any one of statements 1 to 15, wherein each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷,

each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl,

aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S.

17. The compound according to any one of statements 1 to 16, or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S.

18. The compound according to any one of statements 1 to 17, wherein R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclalkyl;

heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 .

19. The compound according to any one of statements 1 to 18, wherein each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$.

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

each R^{17} is independently selected from the group consisting of hydrogen; $-NH_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;

each R^{18} is independently selected from the group consisting of alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

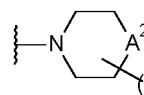
each R^{19} is independently selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

each Z^7 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$, preferably at least one can be oxidized to form at least one $\text{C}=\text{O}$, or $\text{C}=\text{S}$.

20. The compound according to any one of statements 1 to 19, or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$, preferably at least one can be oxidized to form at least one $\text{C}=\text{O}$, or $\text{C}=\text{S}$.

21. The compound according to any one of statements 1 to 14, wherein R^2 and R^3 form together



with the nitrogen to which they are attached a moiety of formula

A^2 is selected from the group consisting of O; NR^9 ; NH; $\text{CR}^{10}\text{R}^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl; heterocyclcarbonylalkyl; heterocyclcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ; each Z^4 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$, preferably at least one can be oxidized to form at least one $\text{C}=\text{O}$, or $\text{C}=\text{S}$;

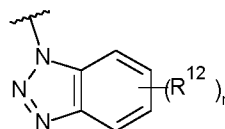
R^{10} is selected from the group consisting of halo, alkyl, alkenyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{OR}^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-\text{SR}^{19}$; cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ; each Z^5 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano;

hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ; each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$.

22. The compound according to any one of claims 1 to 14, wherein R^2 and R^3 form together with the

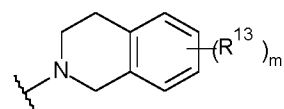


nitrogen to which they are attached a moiety of formula ; wherein,

n is an integer selected from 0, 1, 2, or 3;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$.

23. The compound according to any one of statements 1 to 14, wherein R^2 and R^3 form together



with the nitrogen to which they are attached a moiety of formula ;
wherein,

m is an integer selected from 0, 1, 2, or 3;

R^{13} is selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$.

24. The compound according to any one of statements 1-4, 6, 7, 9, 11-23, wherein,

A^1 is S;

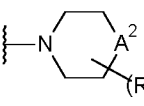
L is selected from the group consisting of $C=O$; S; $*NR^6-NR^7-C(O)**$; $C=S$; and a single bond;

R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from

the group consisting of ; wherein,

A^2 is selected from the group consisting of O; NR^9 ; NH; $CR^{10}R^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

5 R^9 is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

10 R^{10} is selected from the group consisting of halo, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

15 R^{11} is selected from the group consisting of halo, hydrogen, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

20 each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$, preferably at least one can be oxidized to form at least one C=O, or C=S;

25 R^6 is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

30 R^7 is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R^{17} is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R^{18} is independently selected from the group consisting of alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R^{19} is independently selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroarylheterocyclyl, heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached

can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

- 5 each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z³ together with the atom to which they are attached
- 10 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

- each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached
- 15 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;
- 20 each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached
- 25 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

- each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached
- 30 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

- each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached
- 35 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S.

25. The compound according to any one of statements 1-3, 5, 6, 7-23, wherein,

A¹ is O;

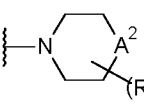
L is selected from the group consisting of C=O; S; NR⁵; *NR⁶-NR⁷-C(O)**; C=S; and a single bond;

R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

R² is selected from the group consisting of arylalkyl; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z³;

or R² and R³ form together with the nitrogen to which they are attached a moiety selected from

the group consisting of ; wherein,

A² is selected from the group consisting of O; NR⁹; NH; CR¹⁰R¹¹; and S;

n is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl; heterocyclcarbonylalkyl; heterocyclcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

R¹⁰ is selected from the group consisting of halo, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclalkyl; heteroaryl;

heteroarylalkyl; carboxyl; -SR¹⁹;
 cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -
 NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be
 unsubstituted or substituted with one or more Z⁵;

5 R¹¹ is selected from the group consisting of halo, hydrogen, alkyl, haloalkyl; haloalkyloxy;
 cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclalkyl;
 heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹;
 cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -
 NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be
 10 unsubstituted or substituted with one or more Z⁶;

each R¹² is independently selected from the group consisting of hydrogen; halo; -NO₂; aryl;
 cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl;
 heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹;
 carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)
 15 R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two R¹² together with the atom to which they
 are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and
 wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl;
 heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or
 S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

20 R⁵ is selected from the group consisting of hydrogen, alkyl; aryl; cycloalkyl; arylalkyl;
 heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁶ is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl;
 heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁷ is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl;
 25 heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl;
 arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one
 carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be
 oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can
 30 be oxidized to form at least one C=O, or C=S;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl;
 alkylaminoalkyl; hydroxyalkyl, aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl;
 heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl,
 aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S,
 35 N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or
 C=S;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroaryheterocyclyl, heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z³ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one

carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

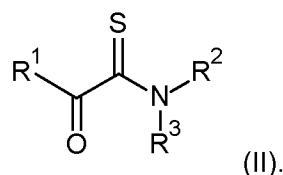
each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

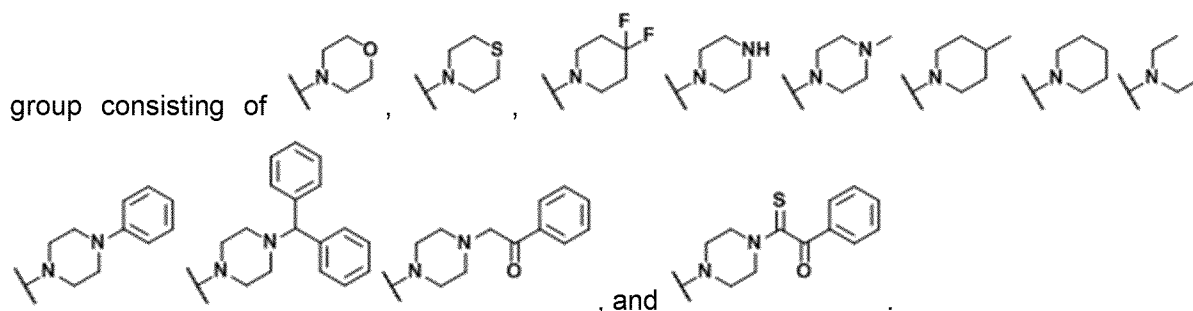
each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl

moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S.

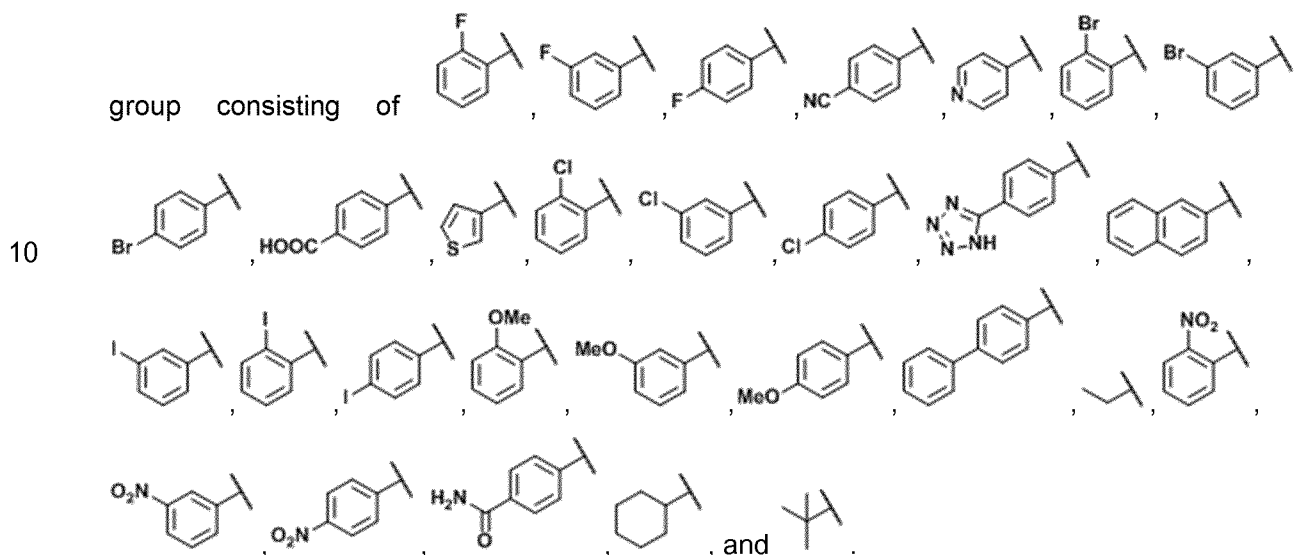
26. The compound according to any one of statements 1-4, 6, 13-25, having formula (II)



27. The compound according to any one of statements 1 to 26, wherein -NR²R³ is selected from the

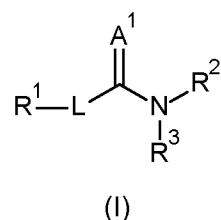


28. The compound according to any one of statements 1 to 27, wherein R¹ is selected from the



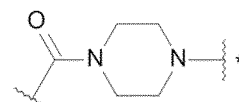
29. A pharmaceutical composition comprising one or more pharmaceutically acceptable excipients and a therapeutically effective amount of a compound according to any one of statements 1 to 28.

30. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use as a medicament,



wherein,

A¹ is selected from the group consisting of S; O; and NR⁴;



L is selected from the group consisting of C=O; S; O; NR⁵; *NR⁶-NR⁷-C(O)**; ** ;

C=S; and a single bond; wherein * represents where L is bound to C=A¹; and ** represents where

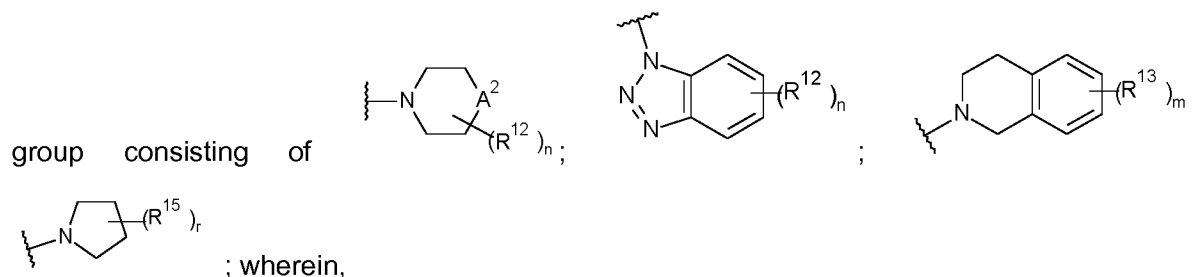
5 L is bound to R¹; and wherein,

R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z³;

15 or R² and R³ form together with the nitrogen to which they are attached a moiety selected from the



A² is selected from the group consisting of O; NR⁹; CR¹⁰R¹¹; and S;

n is an integer selected from 0, 1, 2, or 3;

20 m is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl; heterocyclalkylcarbonylalkyl; heterocyclalkylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

R¹⁰ is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -

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NO_2 ; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{OR}^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-\text{SR}^{19}$; cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-\text{OR}^{18}$; cycloalkyl; arylalkyl; heterocyclylalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R⁷ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; heteroaryheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS

(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

- 5 each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z³ together with the atom to which they are attached can
10 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

- each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can
15 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

- each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -N
25 HS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

- each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -N
30 HS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be
35 oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-N$
 $HS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached
 5 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one
 carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be
 oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A^1 is O; R^1 is heteroaryl, then L is not a
 single bond;

10 and with the proviso that for a compound of formula (I) when A^1 is S; R^1 is heteroarylalkyl or
 arylalkyl; A^2 is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is
 unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is
 15 unsubstituted aryl, then L is not NH;

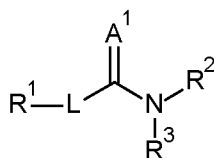
and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is O; R^1 is unsubstituted
 aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is NR^9 or S; R^1 is aryl; then L
 is not S;

20 and with the proviso that said compound is not

- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) morpholine-4-carbodithioate;
- 25 - (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 30 - 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone.

31. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or
 a tautomer thereof, for use as a medicament,

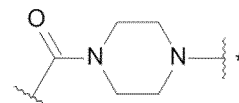


81

(I)

wherein,

A¹ is selected from the group consisting of S; O; and NR⁴;



L is selected from the group consisting of C=O; S; O; NR⁵; *NR⁶-NR⁷-C(O)**; ** ;

5 C=S; and a single bond; wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹; and wherein,

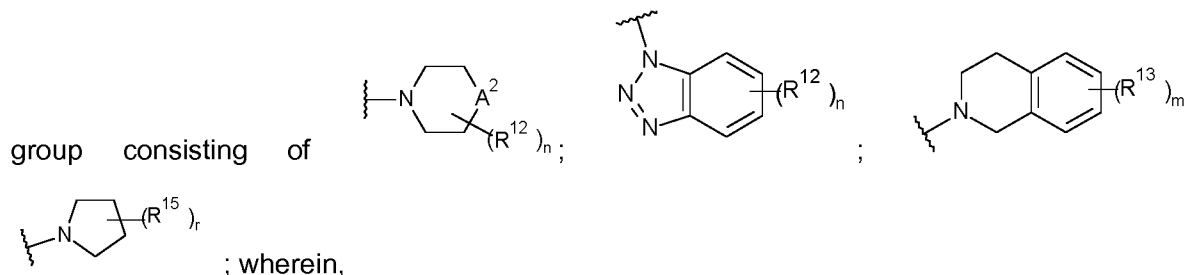
R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

10 R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein

15 each group can be unsubstituted or substituted with one or more Z³;

or R² and R³ form together with the nitrogen to which they are attached a moiety selected from the



A² is selected from the group consisting of O; NR⁹; CR¹⁰R¹¹; and S;

20 n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl; heterocyclcarbonylalkyl; heterocyclcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

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R¹⁰ is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹;

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cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{OR}^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-\text{SR}^{19}$; cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-\text{OR}^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁶ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁷ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

5 each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; 10 alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 15 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, 20 heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl 25 moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or 30 S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; heteroaryheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS 35 (O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^2 together with the atom to which they are attached can
 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom
 5 or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at
 least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 10 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can
 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom
 or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at
 least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

15 each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can
 20 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom
 or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at
 least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 25 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-N$
 $HS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached
 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one
 carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be
 30 oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 35 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-N$
 $HS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached
 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one
 carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be
 oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^7 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;

carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

10 and with the proviso that for a compound of formula (I) when A^1 is O; R^1 is heteroaryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^1 is heteroarylalkyl or arylalkyl; A^2 is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is O; R^1 is unsubstituted aryl, then L is not NH;

20 and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is NR^9 or S; R^1 is aryl; then L is not S;

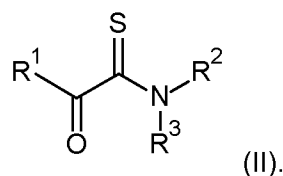
and with the proviso that said compound is not

- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 25 - (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) morpholine-4-carbodithioate;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- 30 - morpholino N-phenylcarbamodithioate;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 35 - 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-[3-[2-(1-piperidyl)-2-thioxo-acetyl]phenyl]acetamide
- N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;

- N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

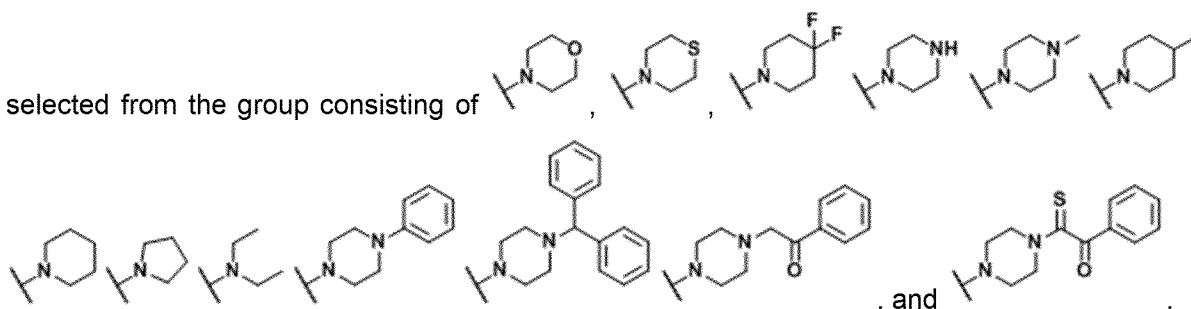
5 32. A compound for use according to any one of statements 30 or 31, wherein said compound is a compound according to any one of statements 1 to 29.

33. The compound for use according to any one of statements 30 to 32, having formula (II)

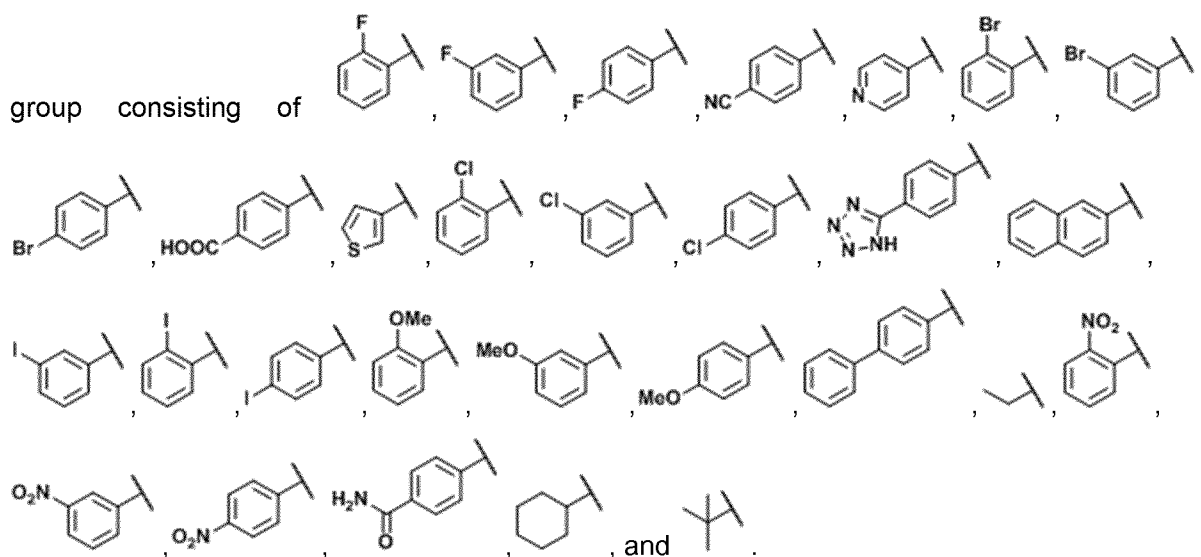


34. The compound for use according to any one of statements 30, 31 or 33, wherein $-\text{NR}^2\text{R}^3$ is

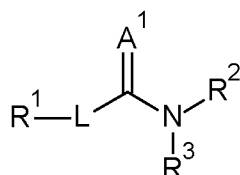
10 selected from the group consisting of



35. The compound for use according to any one of claims 30 to 34, wherein R^1 is selected from the



36. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use in the prevention or treatment of a cellular proliferative disease,

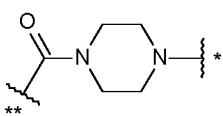
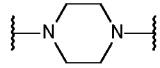


(I)

wherein,

A¹ is selected from the group consisting of S; O; and NR⁴;

L is selected from the group consisting of C=O; S; O; NR⁵; *NR⁶-NR⁷-C(O)**; NR⁶-NR⁷;

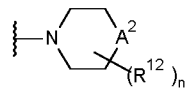
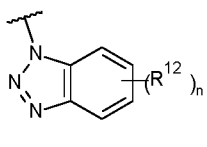
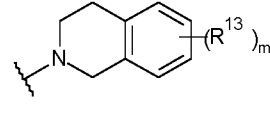
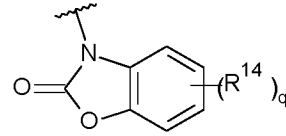
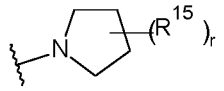
5  ;  ; C=S; a single bond; C=NR⁸; and SO₂; wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹; and wherein,

R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclylalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

10 R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein
15 each group can be unsubstituted or substituted with one or more Z³;

or R² and R³ form together with the nitrogen to which they are attached a moiety selected from the

group consisting of  ;  ;  ;  ;  ; wherein,

A² is selected from the group consisting of O; NR⁹; CR¹⁰R¹¹; and S;

20 n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

q is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be
25 unsubstituted or substituted with one or more Z⁴;

R^{10} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{14} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{14} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl;

heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclylalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^8 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclylalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl;

heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{17} is independently selected from the group consisting of hydrogen; $-NH_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;

each R^{18} is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{19} is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or

5 $S(O)_2$;

each Z^1 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; heteroaryheterocyclyl, $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 10 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$;

each Z^2 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 15 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^2 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 20 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 30 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

35 each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-N$

$\text{HS(O)}_2\text{R}^{20}$; and $-\text{NHC(O)NR}^{16}\text{R}^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O , C=S , N=O , N=S , S=O or S(O)_2 ;

- 5 each Z^6 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C(O)NR}^{16}\text{R}^{17}$; $-\text{C(O)R}^{20}$; $-\text{S(O)R}^{20}$; $-\text{S(O)}_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC(O)R}^{20}$; $-\text{NHS(O)}_2\text{R}^{20}$; and $-\text{NHC(O)NR}^{16}\text{R}^{17}$; or two Z^6 together with the atom to which they are attached
10 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O , C=S , N=O , N=S , S=O or S(O)_2 ;

- each Z^7 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C(O)NR}^{16}\text{R}^{17}$; $-\text{C(O)R}^{20}$; $-\text{S(O)R}^{20}$; $-\text{S(O)}_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC(O)R}^{20}$; $-\text{NHS(O)}_2\text{R}^{20}$; and $-\text{NHC(O)NR}^{16}\text{R}^{17}$; or two Z^7 together with the atom to which they are attached
15 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O , C=S , N=O , N=S , S=O or S(O)_2 ;
20

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A^1 is O; R^1 is heteroaryl, then L is not a single bond;

- and with the proviso that for a compound of formula (I) when A^1 is S; R^1 is heteroarylalkyl; A^2 is O,
25 then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

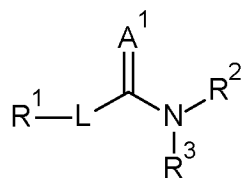
and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

- 30 and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is O; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is NR^9 ; R^1 is aryl; then L is not S.

37. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or
35 a tautomer thereof, for use in the prevention or treatment of a cellular proliferative disease,

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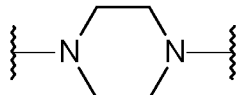
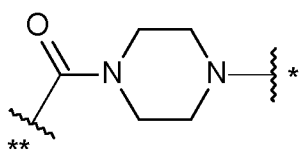


(I)

wherein,

A^1 is selected from the group consisting of S; O; and NR^4 ;

5 L is selected from the group consisting of $\text{C}=\text{O}$; S; O; NR^5 ; $^*\text{NR}^6-\text{NR}^7-\text{C}(\text{O})^{**}$; NR^6-NR^7 ;



; $\text{C}=\text{S}$; a single bond; $\text{C}=\text{NR}^8$; and SO_2 ; wherein *

represents where L is bound to $\text{C}=\text{A}^1$; and ** represents where L is bound to R^1 ; and wherein,

R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group

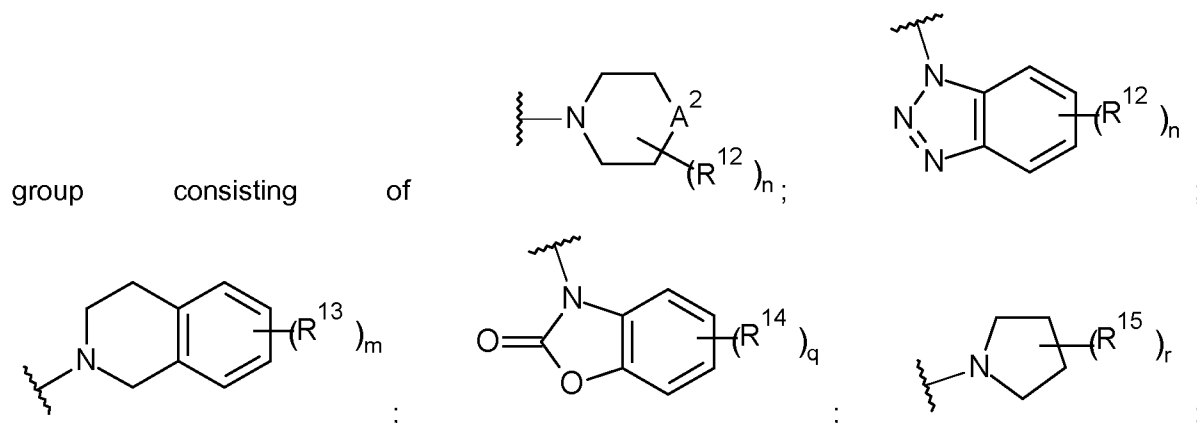
10 can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl;

15 arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from the



20 wherein,

A^2 is selected from the group consisting of O; NR^9 ; $\text{CR}^{10}\text{R}^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

q is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl; heterocyclcarbonylalkyl; heterocyclcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{14} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;

carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{14} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-\text{OR}^{18}$; cycloalkyl; arylalkyl; heterocyclylalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl;

R^8 is selected from the group consisting of alkyl; hydroxyl; $-\text{OR}^{18}$; cycloalkyl; arylalkyl; heterocyclylalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{17} is independently selected from the group consisting of hydrogen; $-\text{NH}_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;

each R^{18} is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; heteroarylalkyl; and cyanoalkyl;

wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; heteroaryheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z³ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can

form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano;

- 5 hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹;
 carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached
 10 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano;

- hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹;
 15 carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached
 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

- 20 each Z⁷ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹;

- carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁷ together with the atom to which they are attached
 25 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

- and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl, then L is not a
 30 single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

- 35 and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is O; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is NR^9 ; R^1 is aryl; then L is not S;

5 and with the proviso that said compound is not

- 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
- 10 - N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;

N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

38. The compound for use according to any one of statements 36 or 37, wherein said compound is a compound according to any one of claims 1 to 30.

39. The compound for use according to any one of statements 36 to 38, wherein A^1 is selected from
15 the group consisting of S; O; preferably A^1 is S;

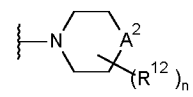
L is selected from the group consisting of C=O; S; and a single bond; preferably C=O, and S, more preferably C=O;

R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; arylalkyl; heterocyclylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 ;

20 R^2 is selected from the group consisting of arylalkyl; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or
25 substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety
wherein,



A^2 is selected from the group consisting of O; NR^9 ; and S;

n is an integer selected from 0, 1, 2, or 3;

30 R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl;
35 heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; -

C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two R¹² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, or C=S;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, or C=S;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, or C=S;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; heteroarylheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered

ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S.

40. The compound for use according to any one of statements 36 to 39, wherein A^1 is S;

L is C=O; or S;

R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; arylalkyl;

wherein each group can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; cycloalkyl; aryl; heterocyclyl; and heteroaryl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; cycloalkyl; aryl; heterocyclylalkyl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted

with one or more Z^3 ;

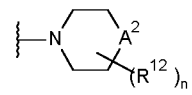
or R^2 and R^3 form together with the nitrogen to which they are attached a moiety wherein,

A^2 is selected from the group consisting of O; NR^9 ; and S;

n is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; alkoxy; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heterocyclyl; or two R^{12} together with the atom to which they are attached can form a



saturated or unsaturated 5-, or 6-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each Z^1 is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkyl; alkoxy, haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; heteroarylheterocyclyl, carboxyl;

each Z^2 is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkyl; alkoxy, haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; carboxyl; or two Z^2 together with the atom to which they are attached can form a

saturated or unsaturated 5-, or 6-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each Z^3 is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkoxy, alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

heterocyclylalkyl; carboxyl; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, or 6-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S;

each Z^4 is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano;

hydroxyl; alkoxy, alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; carboxyl; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, or 6-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, or C=S.

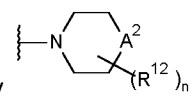
41. The compound for use according to any one of statements 36 to 40, wherein A^1 is S; L is C=O; or S;

R^1 is selected from the group consisting of aryl; heteroaryl; heterocyclyl; alkyl; arylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; cycloalkyl; aryl; and heterocyclyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; cycloalkyl; aryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety wherein,



A^2 is selected from the group consisting of O; NR⁹; and S;

n is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

5 each R¹² is independently selected from the group consisting of hydrogen; halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkoxy; alkyl; haloalkyl; haloalkyloxy; arylalkyl;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkyl; alkoxy, haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; heteroarylheterocyclyl, carboxyl;

10 each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkyl; alkoxy, haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; carboxyl;

each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkoxy, alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

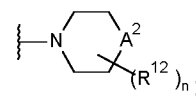
15 heterocyclalkyl; carboxyl;;

each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkoxy, alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; carboxyl.

42. The compound for use according to any one of statements 36 to 41, wherein A¹ is S; L is C=O; 20 or S;

R¹ is selected from the group consisting of aryl; heteroaryl; heterocyclyl; alkyl; arylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

R² and R³ form together with the nitrogen to which they are attached a moiety wherein,



25 A² is selected from the group consisting of O; NR⁹; and S;
n is 0, or 1;

R⁹ is selected from the group consisting of aryl; hydrogen; alkyl; arylalkyl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

30 each R¹² is independently selected from the group consisting of hydrogen; aryl; cycloalkyl; alkoxy; alkyl; arylalkyl;

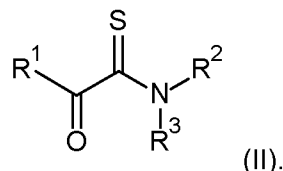
each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkyl; alkoxy, haloalkyl; haloalkyloxy; arylalkyl; heteroaryl, carboxyl;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; alkyl; alkoxy, haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; carboxyl;

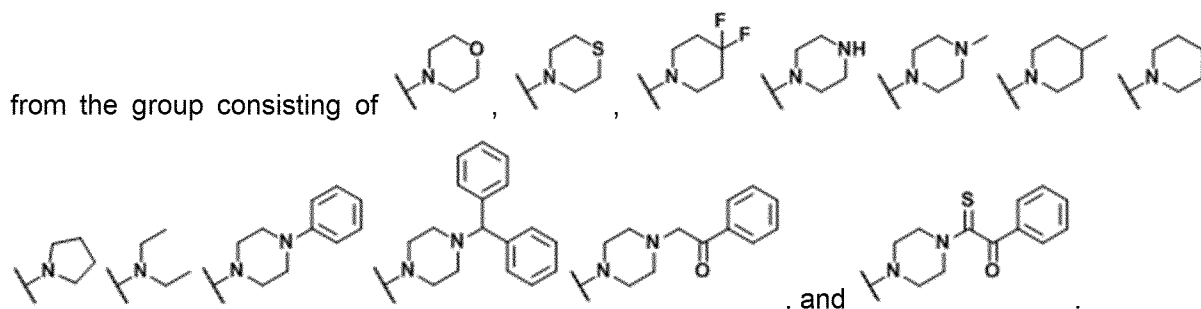
each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; alkoxy, alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; carboxyl;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; alkoxy, alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; carboxyl.

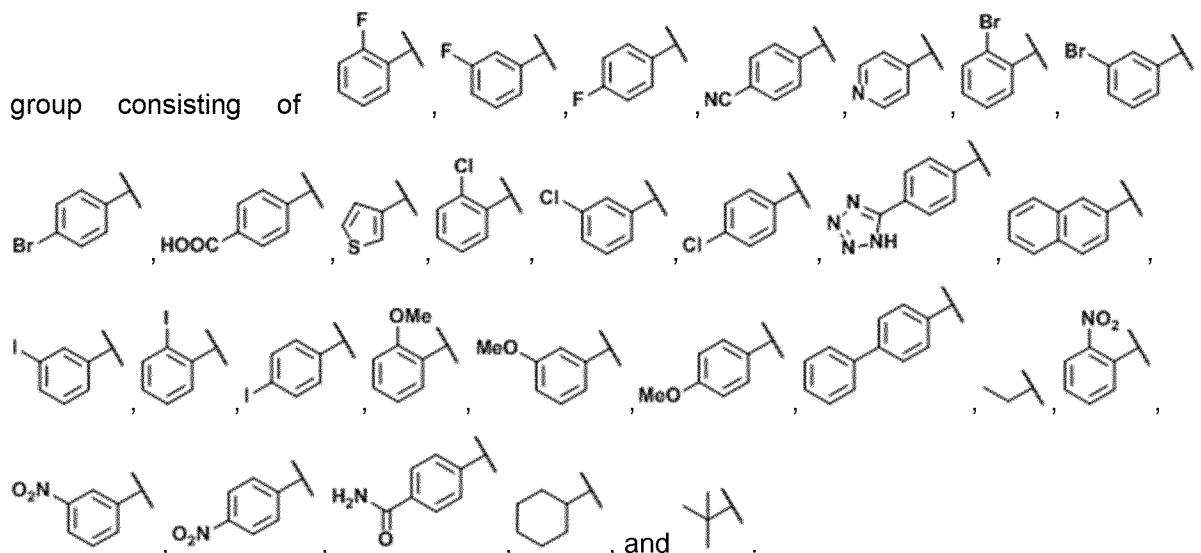
5 43. The compound for use according to any one of statements 36 to 42, having formula (II)



44. The compound for use according to any one of statements 36 to 43, wherein $-NR^2R^3$ is selected



10 45. The compound for use according to any one of claims 36 to 44, wherein R^1 is selected from the



15 46. A pharmaceutical composition according to statement 29 for use in the prevention or treatment of a cellular proliferative disease.

47. The compound for use according to any one of statements 36 to 44, or the pharmaceutical composition for use according to statement 46 wherein said cellular proliferative disease is cancer.

20 48. The compound for use according to statement 47 or the pharmaceutical composition for use according to statement 46 wherein said cancer is selected from the group comprising breast cancer, prostate cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung

cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, vulval
 5 cancer, thyroid cancer, hepatic carcinoma, gastric cancer, melanoma, and neck cancer.

49. A method of treatment of a cellular proliferative disease, comprising administering to a subject in need thereof an effective amount of a compound according to any one of statements 1 to 28, or a pharmaceutical composition according to statement 29.

50. A method for inhibiting serine biosynthesis comprising the step of contacting at least one
 10 enzyme of the serine biosynthetic pathway with an effective amount of a compound according to any one of statements 1 to 28, or a pharmaceutical composition according to statement 29.

51. The method according to claim 50, wherein said at least one enzyme of the serine biosynthetic pathway is selected from the group comprising phosphoglycerate dehydrogenase and phosphoserine aminotransferase 1.

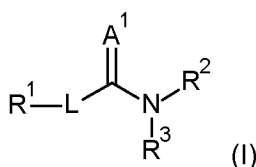
15 52. A method for inhibiting phosphoglycerate dehydrogenase comprising contacting said phosphoglycerate dehydrogenase with an effective amount of a compound according to any one of statements 1 to 28, or as defined in any one of statements 36 to 44.

53. A method for inhibiting phosphoserine aminotransferase 1 comprising contacting said phosphoserine aminotransferase 1 with an effective amount of a compound according to any
 20 one of statements 1 to 28, or as defined in any one of statements 36 to 44.

54. The method according to any one of statements 50 to 53, wherein said method is in vitro.

55. The method according to any one of statements 50 to 53, wherein said method is in vivo.

56. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof,

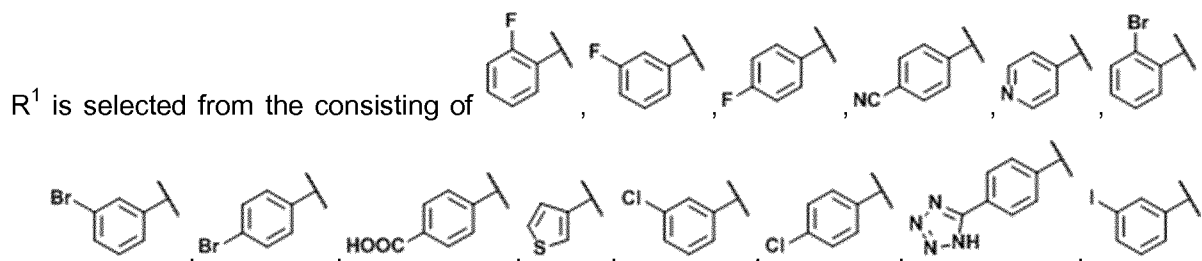


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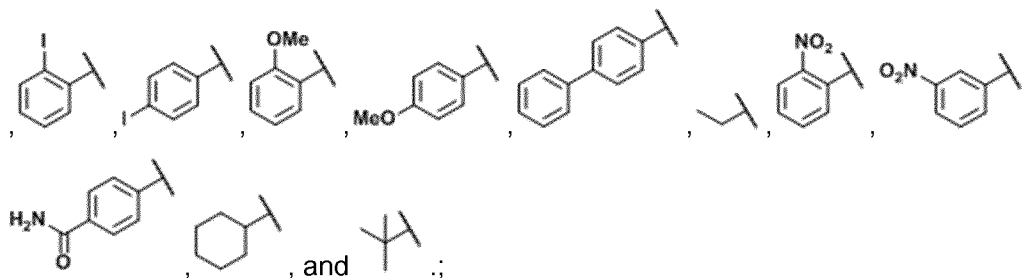
wherein,

A¹ is S;

L is selected from the group consisting of C=O; S; *NR⁶-NR⁷-C(O)**; C=S; and a single bond;



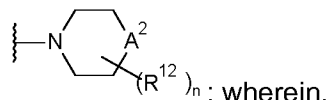
30



R^2 is selected from the group consisting of arylalkyl; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; cycloalkyl; aryl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from



the group consisting of $(\text{N}-\text{C}(\text{R}^{12})\text{A}^2)_n$; wherein,

A^2 is selected from the group consisting of O; NR^9 ; NH; $\text{CR}^{10}\text{R}^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{OR}^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-\text{SR}^{19}$; cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{OR}^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-\text{SR}^{19}$; cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl;

- heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and
- 5 wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;
- R^6 is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;
- 10 R^7 is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;
- each R^{16} is independently selected from the group consisting of hydrogen; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety
- 15 can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;
- each R^{17} is independently selected from the group consisting of hydrogen; $-NH_2$; alkyl; alkylaminoalkyl; hydroxyalkyl, aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl,
- 20 aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;
- or R^{16} and R^{17} form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z^7 ;
- 25 each R^{18} is independently selected from the group consisting of alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;
- 30 each R^{19} is independently selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;
- 35 each R^{20} is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety

can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z³ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z³ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

- each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;
- each Z^7 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$, preferably at least one can be oxidized to form at least one $C=O$, or $C=S$;

with the proviso that said compound is not

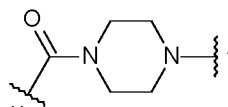
- 2-morpholino-1-(4-phenylphenyl)-2-thioxo-ethanone;
- (3-chlorophenyl)-morpholino-methanethione;
- 1-(4-fluorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-bromophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- (4-phenylphenyl)-(4-phenylpiperazin-1-yl)methanethione;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 4-(2-morpholino-2-thioxo-acetyl)benzoic acid.

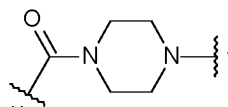
57. The compound according to statement 56, wherein L is $C=O$.

58. The compound according to statement 56, wherein L is S.

59. The compound according to statement 56, wherein L is NR^5 and R^5 is selected from the group consisting of hydrogen, alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl.

60. The compound according to any one of statements 56, wherein L is $*NR^6-NR^7-C(O)**$, wherein * represents where L is bound to $C=A^1$; and ** represents where L is bound to R^1 , R^6 is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; R^7 is selected from the group consisting of hydrogen; alkyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl.

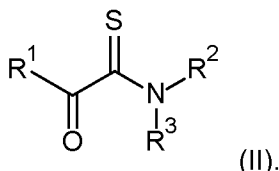


61. The compound according to statement 56, wherein L is  wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹.

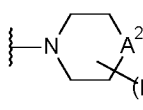
62. The compound according to statement 56, wherein L is C=S.

63. The compound according to statement 56, wherein L is a single bond.

5 64. The compound according to statement 56, having formula (II)



65. The compound according to any one of statements 56 to 65, wherein R² and R³ form together

with the nitrogen to which they are attached a moiety of formula ; wherein,

A² is selected from the group consisting of O; NR⁹; NH; CR¹⁰R¹¹; and S;

10 n is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴; each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂, preferably at least one can be oxidized to form at least one C=O, or C=S;

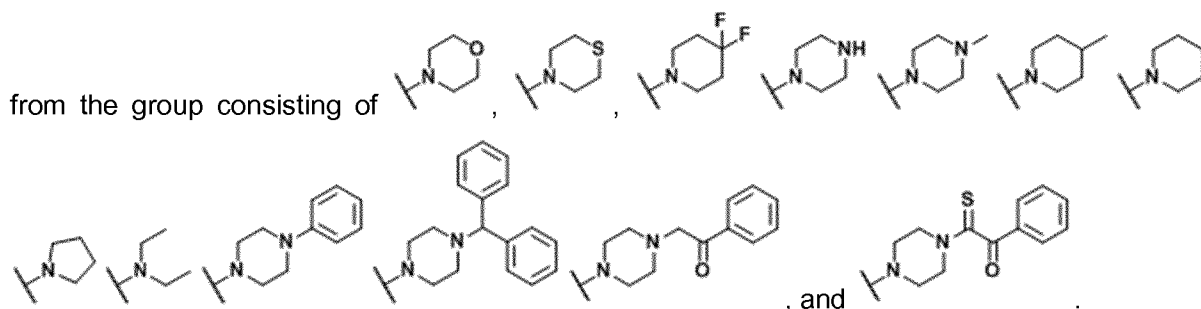
R¹⁰ is selected from the group consisting of halo, alkyl, alkenyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be unsubstituted or substituted with one or more Z⁵; each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹;

carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$, preferably at least one can be oxidized to form at least one $\text{C}=\text{O}$, or $\text{C}=\text{S}$;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{OR}^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-\text{SR}^{19}$, cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ; each Z^6 is independently selected from the group consisting of halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$, alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$, preferably at least one can be oxidized to form at least one $\text{C}=\text{O}$, or $\text{C}=\text{S}$;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$, preferably at least one can be oxidized to form at least one $\text{C}=\text{O}$, or $\text{C}=\text{S}$.

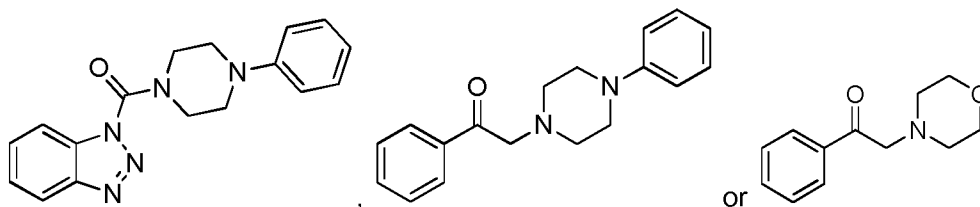
66. The compound for use according to any one of statements 56 to 66, wherein $-\text{NR}^2\text{R}^3$ is selected



67. A pharmaceutical composition comprising one or more pharmaceutically acceptable excipients and a therapeutically effective amount of a compound according to any one of statements 56 to 66.

68. A compound according to any one of statements 56 to 66 for use as a medicament.

5 69. A compound according to any one of statements 56 to 66 or a compound selected from:



for use in the prevention or treatment of a cellular proliferative disease.

70. A pharmaceutical composition according to statement 67 for use in the prevention or treatment of a cellular proliferative disease.

10 71. The compound for use according to statement 69, or the pharmaceutical composition for use according to statement 70, wherein said cellular proliferative disease is cancer.

72. The compound for use according to statement 69 or the pharmaceutical composition for use according to statement 70, wherein said cancer is selected from the group comprising breast cancer, prostate cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, vulval cancer, thyroid cancer, hepatic carcinoma, gastric cancer, melanoma, and neck cancer.

20 73. A method of treatment of a cellular proliferative disease, comprising administering to a subject in need thereof an effective amount of a compound according to any one of statements 56 to 66, or a pharmaceutical composition according to statement 67.

74. A method for inhibiting serine biosynthesis comprising the step of contacting at least one enzyme of the serine biosynthetic pathway with an effective amount of a compound according to
25 any one of statements 56 to 66, or a pharmaceutical composition according to statement 67.

75. The method according to claim 74, wherein said at least one enzyme of the serine biosynthetic pathway is selected from the group comprising phosphoglycerate dehydrogenase and phosphoserine aminotransferase 1.

76. A method for inhibiting phosphoglycerate dehydrogenase comprising contacting said
30 phosphoglycerate dehydrogenase with an effective amount of a compound according to any one of statements 56 to 66.

77. A method for inhibiting phosphoserine aminotransferase 1 comprising contacting said phosphoserine aminotransferase 1 with an effective amount of a compound according to any one of statements 56 to 66.
78. The method according to any one of statements 74 to 77, wherein said method is in vitro.
- 5 79. The method according to any one of statements 74 to 77, wherein said method is in vivo.
80. The pharmaceutical composition according to any one of statement 29 or 67, comprising at least one immune checkpoint inhibitor.
81. A combination of at least one compound according to any one of statements 1 to 28, 56 to 66, or at least one compound for use according to any one of statements 30 to 48, 68 to 72, with at
10 least one immune check point inhibitor.
82. The compound for use according to any one of claims statements 30 to 48, 68 to 72, together with at least one immune checkpoint inhibitor.
83. The pharmaceutical composition according to statement 80, the combination according to statement 81 or the compound for use according to statement 82, wherein the at least one
15 immune checkpoint inhibitor is an inhibitor as described in any one of WO2017011666, IMS health Institute global Oncology report June 2016, Nature Reviews Clinical Oncology 2013 (13) 143-158, and Clin. Cancer research 2013 (19) 1021-1034.
84. The pharmaceutical composition according to statement 80, the combination according to statement 81 or the compound for use according to statement 82, wherein the at least one
20 immune checkpoint inhibitor is selected from the group comprising PD1, PD-L1, CTLA4, IDO, TDO, CD122, CD27, GITR, CD40, OX40, CD73, CD137, 4-1BB, CSF1R, LAG3, KIR, TIM-3, IL2, ADA, STING and TIGIT.
85. The compound for use according to claim 82, comprising either the administration of the compound of the present invention prior to immune checkpoint therapy, administration
25 concomittant with immune checkpoint therapy, or administration after immune checkpoint therapy.
86. A combination of at least one compound according to any one of statements 1 to 28, 56 to 66, or at least one compound for use according to any one of statements 30 to 48, 68 to 72, with CAR-T cell therapeutic strategy.
- 30 The present invention includes all possible stereoisomers compounds of formulae (I) or (II) and any subgroup thereof and includes not only racemic compounds but the individual enantiomers as well. When a compound is desired as a single enantiomer, such may be obtained by stereospecific synthesis, by resolution of the final product or any convenient intermediate, or by chiral chromatographic methods as each are known in the art. Resolution of the final product, an
35 intermediate, or a starting material may be effected by any suitable method known in the art. See, for example, Stereochemistry of Organic Compounds by E. L. Eliel, S. H. Wilen, and L. N. Mander (Wiley- Interscience, 1994), incorporated by reference with regard to stereochemistry.

The compounds of the invention may be in the form of pharmaceutically acceptable salts, as generally described below. Some preferred, but non-limiting examples of suitable pharmaceutically acceptable organic and/or inorganic acids are as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, acetic acid and citric acid, as well as other pharmaceutically acceptable acids known per se (for which reference is made to the prior art referred to below).

When the compounds of the invention contain an acidic group as well as a basic group the compounds of the invention may also form internal salts, and such compounds are within the scope of the invention. When the compounds of the invention contain a hydrogen-donating heteroatom (e.g. NH), the invention also covers salts and/or isomers formed by transfer of said hydrogen atom to a basic group or atom within the molecule.

Pharmaceutically acceptable salts of the compounds of formulae (I) or (II) and any subgroup thereof include the acid addition and base salts thereof. Suitable acid addition salts are formed from acids which form non-toxic salts. Examples include the acetate, adipate, aspartate, benzoate, besylate, bicarbonate/carbonate, bisulfate/sulfate, borate, camsylate, citrate, cyclamate, edisylate, esylate, formate, fumarate, gluceptate, gluconate, glucuronate, hexafluorophosphate, hibenzate, hydrochloride/chloride, hydrobromide/bromide, hydroiodide/iodide, isethionate, lactate, malate, maleate, malonate, mesylate, methylsulphate, naphthylate, 2-napsylate, nicotinate, nitrate, orotate, oxalate, palmitate, palmoate, phosphate/hydrogen phosphate/dihydrogen phosphate, pyroglutamate, saccharate, stearate, succinate, tannate, tartrate, tosylate, trifluoroacetate and xinofoate salts.

Suitable base salts are formed from bases which form non-toxic salts. Examples include the aluminium, arginine, benzathine, calcium, choline, diethylamine, diolamine, glycine, lysine, magnesium, meglumine, olamine, potassium, sodium, tromethamine and zinc salts. Hemisalts of acids and bases may also be formed, for example, hemisulphate and hemicalcium salts. For a review on suitable salts, see Handbook of Pharmaceutical Salts: Properties, Selection, and Use by Stahl and Wermuth (Wiley-VCH, 2002), incorporated herein by reference.

The compounds of the invention may exist in a continuum of solid states ranging from fully amorphous to fully crystalline. The term 'amorphous' refers to a state in which the material lacks long range order at the molecular level and, depending upon temperature, may exhibit the physical properties of a solid or a liquid. Typically such materials do not give distinctive X-ray diffraction patterns and, while exhibiting the properties of a solid, are more formally described as a liquid. Upon heating, a change from solid to liquid properties occurs which is characterized by a change of state, typically second order ('glass transition'). The term 'crystalline' refers to a solid phase in which the material has a regular ordered internal structure at the molecular level and gives a distinctive X-ray diffraction pattern with defined peaks. Such materials when heated sufficiently will also exhibit the properties of a liquid, but the change from solid to liquid is characterized by a phase change, typically first order ('melting point').

Pharmaceutically acceptable salts of compounds of formulae (I) or (II) may be prepared by one or more of these methods:

(i) by reacting the compound of formulae (I) or (II) with the desired acid;

(ii) by reacting the compound of formulae (I) or (II) with the desired base;

(iii) by removing an acid- or base-labile protecting group from a suitable precursor of the compound of formulae (I) or (II) or by ring-opening a suitable cyclic precursor, for example, a lactone or lactam,

5 using the desired acid; or

(iv) by converting one salt of the compound of formulae (I) or (II) to another by reaction with an appropriate acid or by means of a suitable ion exchange column.

All these reactions are typically carried out in solution. The salt, may precipitate from solution and be collected by filtration or may be recovered by evaporation of the solvent. The degree of ionization in

10 the salt may vary from completely ionized to almost non-ionized.

The compounds of the invention may also exist in unsolvated and solvated forms. The term 'solvate' is used herein to describe a molecular complex comprising the compound of the invention and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is employed when said solvent is water.

15 A currently accepted classification system for organic hydrates is one that defines isolated site, channel, or metal-ion coordinated hydrates - see Polymorphism in Pharmaceutical Solids by K. R. Morris (Ed. H. G. Britain, Marcel Dekker, 1995), incorporated herein by reference. Isolated site hydrates are ones in which the water molecules are isolated from direct contact with each other by intervening organic molecules. In channel hydrates, the water molecules lie in lattice channels where
20 they are next to other water molecules. In metal-ion coordinated hydrates, the water molecules are bonded to the metal ion.

When the solvent or water is tightly bound, the complex will have a well-defined stoichiometry independent of humidity. When, however, the solvent or water is weakly bound, as in channel solvates and hygroscopic compounds, the water/solvent content will be dependent on humidity and

25 drying conditions. In such cases, non-stoichiometry will be the norm.

Also included within the scope of the invention are multi-component complexes (other than salts and solvates) wherein the drug and at least one other component are present in stoichiometric or non-stoichiometric amounts. Complexes of this type include clathrates (drug- host inclusion complexes) and co-crystals. The latter are typically defined as crystalline complexes of neutral molecular
30 constituents which are bound together through non-covalent interactions, but could also be a complex of a neutral molecule with a salt. Co-crystals may be prepared by melt crystallization, by recrystallization from solvents, or by physically grinding the components together - see Chem Commun, 17, 1889-1896, by O. Almarsson and M. J. Zaworotko (2004), incorporated herein by reference. For a general review of multi-component complexes, see J Pharm Sci, 64 (8), 1269-1288,

35 by Haleblan (August 1975), incorporated herein by reference.

The compounds of the invention may also exist in a mesomorphic state (mesophase or liquid crystal) when subjected to suitable conditions. The mesomorphic state is intermediate between the true

crystalline state and the true liquid state (either melt or solution). Mesomorphism arising as the result of a change in temperature is described as 'thermotropic' and that resulting from the addition of a second component, such as water or another solvent, is described as 'lyotropic'. Compounds that have the potential to form lyotropic mesophases are described as 'amphiphilic' and consist of
5 molecules which possess an ionic (such as $-\text{COO}^-\text{Na}^+$, $-\text{COO}^-\text{K}^+$, or $-\text{SO}_3^-\text{Na}^+$) or non-ionic (such as $-\text{N}^+\text{N}^+(\text{CH}_3)_3$) polar head group. For more information, see Crystals and the Polarizing Microscope by N. H. Hartshorne and A. Stuart, 4th Edition (Edward Arnold, 1970), incorporated herein by reference.

All references to compounds of formulae (I) or (II) or any subgroups thereof include references to salts, solvates, multi- component complexes and liquid crystals thereof and to solvates, multi-
10 component complexes and liquid crystals of salts thereof.

The compounds of the invention include compounds of formulae (I) or (II) or any subgroups thereof as hereinbefore defined, including all polymorphs and crystal habits thereof, prodrugs and isomers thereof (including optical, geometric and tautomeric isomers) as hereinafter defined and isotopically-labeled compounds of formulae (I) or (II).

15 In addition, although generally, with respect to the salts of the compounds of the invention, pharmaceutically acceptable salts are preferred, it should be noted that the invention in its broadest sense also included non-pharmaceutically acceptable salts, which may for example be used in the isolation and/or purification of the compounds of the invention. For example, salts formed with optically active acids or bases may be used to form diastereoisomeric salts that can facilitate the
20 separation of optically active isomers of the compounds of formula (I) or (II) above.

Where a compound of formulae (I) or (II) or any subgroup thereof contains an alkenyl or alkenylene group, geometric cis/trans (or Z/E) isomers are possible. Where structural isomers are interconvertible via a low energy barrier, tautomeric isomerism ('tautomerism') can occur. This can take the form of proton tautomerism in compounds of formula (I) containing, for example, an imino,
25 keto, or oxime group, or so-called valence tautomerism in compounds which contain an aromatic moiety. It follows that a single compound may exhibit more than one type of isomerism.

Included within the scope of the present invention are all stereoisomers, diastereomers, geometric isomers and tautomeric forms of the compounds of formula (I) or (II) or any subgroups thereof, including compounds exhibiting more than one type of isomerism, and mixtures of one or more
30 thereof. Also included are acid addition or base salts wherein the counterion is optically active, for example, *d*-lactate or *l*-lysine, or racemic, for example, *dl*- tartrate or *dl*-arginine.

Cis/trans isomers may be separated by conventional techniques well known to those skilled in the art, for example, chromatography and fractional crystallization.

Conventional techniques for the preparation/isolation of individual enantiomers include chiral
35 synthesis from a suitable optically pure precursor or resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high performance liquid chromatography (HPLC).

The compounds of formulae (I) or (II) or any subgroups thereof may be prepared as described in the experimental section below using methods and chemistries with which those skilled in the art shall be familiar.

Generally, the compounds of the invention are prepared from the intermediates described hereinafter which may be reacted with complementary reactive molecules so as to form the desired compound.

The present invention also encompasses processes for the preparation of compounds formula (I) and any subgroup thereof. In the reactions described, it can be necessary to protect reactive functional groups, for example hydroxy, amino, or carboxy groups, where these are desired in the final product, to avoid their unwanted participation in the reactions. Conventional protecting groups can be used in accordance with standard practice, for example, see T. W. Greene and P. G. M. Wuts in "Protective Groups in Organic Chemistry", John Wiley and Sons, 1999. Protected forms of the inventive compounds are included within the scope of the present invention. It will also be clear to the skilled person that compounds of the invention in which one or more functional groups have been protected with suitable functional groups can find use as intermediates in the production and/or synthesis of the compounds of the invention, and as such form a further aspect of the invention.

The compounds formula (I), the subgroups thereof and their pharmaceutically acceptable salts can be prepared as described hereunder.

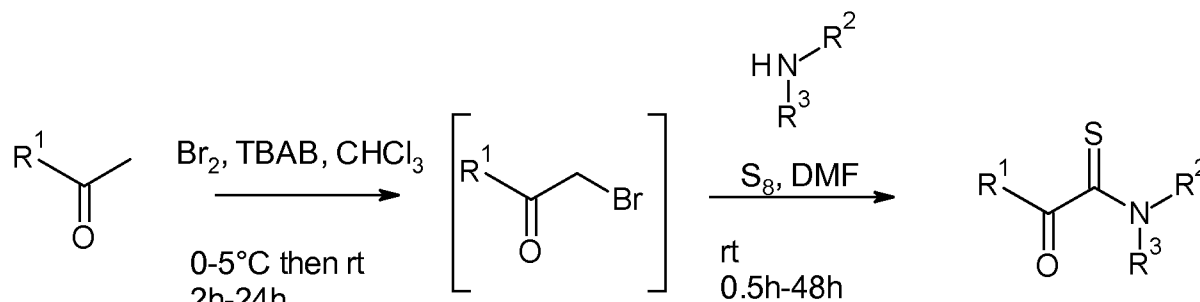
In the general schemes described below, all substituents are defined as in the general formula (I), or any subgroups thereof, unless otherwise mentioned or indicated.

The present compounds of formula (I) and their pharmaceutically acceptable salts can be prepared by methods known in the art, for example, by processes described below, which process comprises coupling a compound of formula **XI** with a compound of formula **XII**:



wherein LG is a leaving group. The present invention therefore encompasses a method for preparing a compound of formula (I) comprising the step of contacting a compound of formula XI with a compound of formula XII.

In some preferred embodiments, the present invention provides a method for preparing a compound of formula (II) as depicted in scheme 2.



Scheme 2

To a stirred solution of ketone derivative in chloroform was added dropwise a solution of dibromine in chloroform, in the presence of tetrabutylammonium bromide. After about 2 hours, the solvent was
 5 evaporated in vacuo to give a crude oil consisting mainly of 2-bromo-1-(substituted)-ethanone compound. The mixture was used without purification in the next step. To the commercial or synthesized 2-bromo-1-(substituted)-ethanone derivative were added in sequence DMF, cyclooctasulfur (S₈) and morpholine. The mixture was then stirred at room temperature. After completion of the reaction, the reaction mixture was quenched with distilled water to give a
 10 precipitate which was further washed with distilled water.

The present invention encompasses compounds according to the invention, as well as the compounds obtained by the methods of the invention. The present invention also encompasses pharmaceutical composition comprising at least one compound of the present invention. The present invention also encompasses pharmaceutical composition comprising at least one compound of the
 15 invention and at least one carrier, excipient or diluent acceptable for pharmaceutical purposes.

In some embodiments, the present invention relates to a compound of formulae (I) or (II), or any subgroups thereof, for use in the prevention and/or treatment of a cellular proliferative disease.

In some embodiments, the present invention relates to the use of at least one compound of formulae (I) or (II), or any subgroups thereof, in the preparation of a medicament for use in the prevention
 20 and/or treatment of a cellular proliferative disease.

In some embodiments, the present invention relates to a method of prevention and/or of treatment of a cellular proliferative disease, comprising administering to a subject in need thereof an effective amount of at least one compound of formulae (I) or (II), or any subgroups thereof, or a pharmaceutical composition comprising said at least one compound of formulae (I) or (II) or any
 25 subgroups thereof.

By "cellular proliferation disorder" is meant a disorder associated with abnormal cell growth. Exemplary cell proliferative disorders include cancer (e.g., benign and malignant), obesity, benign prostatic hyperplasia, psoriasis, abnormal keratinization, lymphoproliferative disorders, rheumatoid arthritis, arteriosclerosis, restenosis, diabetic retinopathy, retrolental fibrioplasia, neovascular
 30 glaucoma, angiofibromas, hemangiomas, Kaposi's sarcoma, and neurodegenerative disorders.

In some embodiments, the present invention relates to a compound of formulae (I) or (II), or any subgroups thereof, for use in the prevention and/or treatment of cancer.

In some embodiments, the present invention relates to the use of at least one compound of formulae (I) or (II), or any subgroups thereof, in the preparation of a medicament for use in the prevention
5 and/or treatment of cancer.

In some embodiments, the present invention relates to a method of prevention and/or of treatment of cancer, comprising administering to a subject in need thereof an effective amount of at least one compound of formulae (I) or (II), or any subgroups thereof, or a pharmaceutical composition comprising said at least one compound of formulae (I) or (II) or any subgroups thereof.

10 By "cancer" is meant the physiological condition in mammals that is typically characterized by abnormal cell growth. Included in this definition are benign and malignant cancers, as well as dormant tumors or micro-metastases. Examples of cancer include, but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia. More particular examples of such cancers include, e.g., prostate cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer,
15 adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, vulval cancer, thyroid cancer, hepatic carcinoma, gastric cancer, melanoma, and various types of
20 head and neck cancer.

The term "subject" as used herein refers to a mammal. The subject will preferably be a human, but may also be a domestic livestock, laboratory or pet animals.

In some embodiments, at least one compound of formulae (I) or (II) is used (for the preparation of a medicament) for preventing and/or treating a disease selected from the group comprising breast
25 cancer, prostate cancer, squamous cell cancer, small-cell lung cancer, non-small-cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, vulval cancer, thyroid
30 cancer, hepatic carcinoma, gastric cancer, melanoma, and neck cancer.

As used herein, the term "effective amount" means that amount of a drug or pharmaceutical agent that will elicit the biological or medical response of a tissue, system, animal, or human that is being sought, for instance, by a researcher or clinician.

The term "therapeutically effective amount" means any amount which, as compared to a
35 corresponding subject who has not received such amount, results in improved treatment, healing, prevention, or amelioration of a disease, disorder, or side effect, or a decrease in the rate of advancement of a disease or disorder. The term also includes within its scope amounts effective to enhance normal physiological function.

For use in therapy, therapeutically effective amounts of a compound of formula (I) or (II), as well as stereoisomers, tautomers, racemics, salts, hydrates or solvates thereof, may be administered as the raw chemical. Additionally, the active ingredient may be presented as a pharmaceutical composition.

Accordingly, the invention further provides pharmaceutical compositions that include effective
5 amounts of compounds of formulae (I) or (II), or stereoisomers, tautomers, racemics, salts, hydrates or solvates thereof, and one or more pharmaceutically acceptable carriers, diluents, or excipients. The compounds of formulae (I) or (II) or stereoisomers, tautomers, racemics, salts, hydrates or solvates thereof, are as herein described.

The compounds according to the invention may be administered as the sole active ingredient or
10 together, i.e. in a fixed or free combination, with other therapeutic agents used in clinical practice for the treatment of those diseases listed above.

The compounds according to the invention and the other pharmaceutical active agent(s) may be administered together or separately and, when administered separately, administration may occur simultaneously or sequentially, in any order. The amounts of the compounds according to the
15 invention and the other pharmaceutically active agent (s) and the relative timings of administration will be selected in order to achieve the desired combined therapeutic effect. The administration in combination of a compound of formulae (I) or (II) or a stereoisomer, tautomer, racemic, salt, hydrate or solvate thereof, with other treatment agents may be in combination by administration concomitantly in: (1) a unitary pharmaceutical composition including both compounds; or (2)
20 separate pharmaceutical compositions each including one of the compounds. Alternatively, the combination may be administered separately in a sequential manner wherein one treatment agent is administered first and the other second or vice versa. Such sequential administration may be close in time or remote in time.

For pharmaceutical use, the compounds of the invention may be used as a free acid or base, and/or
25 in the form of a pharmaceutically acceptable acid-addition and/or base-addition salt (e.g. obtained with non-toxic organic or inorganic acid or base), in the form of a hydrate, solvate and/or complex, and/or in the form of a pro-drug or pre-drug, such as an ester. As used herein and unless otherwise stated, the term "solvate" includes any combination which may be formed by a compound of this invention with a suitable inorganic solvent (e.g. hydrates) or organic solvent, such as but not limited
30 to alcohols, ketones, esters and the like. Such salts, hydrates, solvates, etc. and the preparation thereof will be clear to the skilled person; reference is for instance made to the salts, hydrates, solvates, etc. described in US-A-6,372,778, US-A-6,369,086, US-A-6,369,087 and US-A-6,372,733.

The pharmaceutically acceptable salts of the compounds according to the invention, i.e. in the form of water-, oil-soluble, or dispersible products, include the conventional non-toxic salts or the
35 quaternary ammonium salts which are formed, e.g., from inorganic or organic acids or bases. Examples of such acid addition salts include acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate,

glycerophosphate, hemisulfate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethanesulfonate, lactate, maleate, methanesulfonate, 2-naphthalene-sulfonate, nicotinate, oxalate, palmoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, and undecanoate. Base salts include ammonium salts, alkali metal
5 salts such as sodium and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases such as dicyclohexylamine salts, N-methyl-D-glucamine, and salts with amino acids such as arginine, lysine, and so forth. In addition, the basic nitrogen-containing groups may be quaternized with such agents as lower alkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl;
10 and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl-bromides and others. Other pharmaceutically acceptable salts include the sulfate salt ethanolate and sulfate salts.

Generally, for pharmaceutical use, the compounds of the inventions may be formulated as a pharmaceutical preparation comprising at least one compound of the invention and at least one
15 pharmaceutically acceptable carrier, diluent or excipient and/or adjuvant, and optionally one or more further pharmaceutically active compounds.

By means of non-limiting examples, such a formulation may be in a form suitable for oral administration, for parenteral administration (such as by intravenous, intramuscular or subcutaneous injection or intravenous infusion), for topical administration (including ocular), for administration by
20 inhalation, by a skin patch, by an implant, by a suppository, etc. Such suitable administration forms – which may be solid, semi-solid or liquid, depending on the manner of administration – as well as methods and carriers, diluents and excipients for use in the preparation thereof, will be clear to the skilled person; reference is again made to for instance US-A-6,372,778, US-A-6,369,086, US-A-6,369,087 and US-A-6,372,733, as well as to the standard handbooks, such as the latest edition of
25 Remington's Pharmaceutical Sciences.

Some preferred, but non-limiting examples of such preparations include tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrups, aerosols, ointments, cremes, lotions, soft and hard gelatin capsules, suppositories, drops, sterile injectable solutions and sterile packaged powders (which are usually reconstituted prior to use) for administration as a bolus
30 and/or for continuous administration, which may be formulated with carriers, excipients, and diluents that are suitable per se for such formulations, such as lactose, dextrose, sucrose, sorbitol, mannitol, starches, gum acacia, calcium phosphate, alginates, tragacanth, gelatin, calcium silicate, microcrystalline cellulose, polyvinylpyrrolidone, polyethylene glycol, cellulose, (sterile) water, methylcellulose, methyl- and propylhydroxybenzoates, talc, magnesium stearate, edible oils,
35 vegetable oils and mineral oils or suitable mixtures thereof. The formulations can optionally contain other pharmaceutically active substances (which may or may not lead to a synergistic effect with the compounds of the invention) and other substances that are commonly used in pharmaceutical formulations, such as lubricating agents, wetting agents, emulsifying and suspending agents,

dispersing agents, desintegrants, bulking agents, fillers, preserving agents, sweetening agents, flavoring agents, flow regulators, release agents, etc.. The compositions may also be formulated so as to provide rapid, sustained or delayed release of the active compound(s) contained therein, for example using liposomes or hydrophilic polymeric matrices based on natural gels or synthetic
5 polymers. In order to enhance the solubility and/or the stability of the compounds of a pharmaceutical composition according to the invention, it can be advantageous to employ α -, β - or γ -cyclodextrins or their derivatives. In addition, co-solvents such as alcohols may improve the solubility and/or the stability of the compounds. In the preparation of aqueous compositions, addition of salts of the compounds of the invention can be more suitable due to their increased water solubility.

- 10 Appropriate cyclodextrins are α -, β - or γ -cyclodextrins (CDs) or ethers and mixed ethers thereof wherein one or more of the hydroxyl groups of the anhydroglucose units of the cyclodextrin are substituted with alkyl, particularly methyl, ethyl or isopropyl, e.g. randomly methylated β -CD; hydroxyalkyl, particularly hydroxyethyl, hydroxypropyl or hydroxybutyl; carboxyalkyl, particularly carboxymethyl or carboxyethyl; alkylcarbonyl, particularly acetyl; alkoxyalkyl or
15 carboxyalkoxyalkyl, particularly carboxymethoxypropyl or carboxyethoxypropyl; alkylcarbonyloxyalkyl, particularly 2-acetyloxypropyl. Especially noteworthy as complexants and/or solubilizers are β -CD, randomly methylated β -CD, 2,6-dimethyl- β -CD, 2-hydroxyethyl- β -CD, 2-hydroxyethyl- γ -CD, 2-hydroxypropyl- γ -CD and (2-carboxymethoxy)propyl- β -CD, and in particular 2-hydroxypropyl- β -CD (2-HP- β -CD). The term mixed ether denotes cyclodextrin derivatives wherein
20 at least two cyclodextrin hydroxyl groups are etherified with different groups such as, for example, hydroxypropyl and hydroxyethyl. An interesting way of formulating the compounds in combination with a cyclodextrin or a derivative thereof has been described in EP-A-721,331. Although the formulations described therein are with antifungal active ingredients, they are equally interesting for formulating the compounds. Said formulations may also be rendered more palatable by adding
25 pharmaceutically acceptable sweeteners and/or flavors. In particular, the present invention encompasses a pharmaceutical composition comprising an effective amount of a compound according to the invention with a pharmaceutically acceptable cyclodextrin. The present invention also encompasses cyclodextrin complexes consisting of a compound according to the invention and a cyclodextrin.
- 30 The preparations may be prepared in a manner known per se, which usually involves mixing the at least one compound according to the invention with the one or more pharmaceutically acceptable carriers, and, if desired, in combination with other pharmaceutical active compounds, when necessary under aseptic conditions. Reference is again made to US-A-6,372,778, US-A-6,369,086, US-A-6,369,087 and US-A-6,372,733 and the further prior art mentioned above, as well as to the
35 standard handbooks, such as the latest edition of Remington's Pharmaceutical Sciences.

The pharmaceutical preparations of the invention are preferably in a unit dosage form, and may be suitably packaged, for example in a box, blister, vial, bottle, sachet, ampoule or in any other suitable single-dose or multi-dose holder or container (which may be properly labeled); optionally with one or

more leaflets containing product information and/or instructions for use. Generally, such unit dosages will contain between 1 and 1000 mg, and usually between 5 and 500 mg, of the at least one compound of the invention, e.g. about 10, 25, 50, 100, 200, 300 or 400 mg per unit dosage

The compounds can be administered by a variety of routes including the oral, ocular, rectal, 5 transdermal, subcutaneous, intravenous, intramuscular or intranasal routes, depending mainly on the specific preparation used and the condition to be treated or prevented, and with oral and intravenous administration usually being preferred. The at least one compound of the invention will generally be administered in an "effective amount", by which is meant any amount of a compound of the formulae (I) or (II) above that, upon suitable administration, is sufficient to achieve the desired 10 therapeutic or prophylactic effect in the subject to which it is administered. Usually, depending on the condition to be prevented or treated and the route of administration, such an effective amount will usually be between 0.01 to 1000 mg per kilogram, more often between 0.1 and 500 mg, such as between 1 and 250 mg, for example about 5, 10, 20, 50, 100, 150, 200 or 250 mg, per kilogram body weight day of the patient per day, which may be administered as a single daily dose, divided over 15 one or more daily doses, or essentially continuously, e.g. using a drip infusion. The amount(s) to be administered, the route of administration and the further treatment regimen may be determined by the treating clinician, depending on factors such as the age, gender and general condition of the patient and the nature and severity of the disease/symptoms to be treated. Reference is again made to US-A-6,372,778, US-A-6,369,086, US-A-6,369,087 and US-A-6,372,733 and the further prior art 20 mentioned above, as well as to the standard handbooks, such as the latest edition of Remington's Pharmaceutical Sciences.

In accordance with the method of the present invention, said pharmaceutical composition can be administered separately at different times during the course of therapy or concurrently in divided or single combination forms. The present invention is therefore to be understood as embracing all such 25 regimes of simultaneous or alternating treatment and the term "administering" is to be interpreted accordingly.

For an oral administration form, the compositions of the present invention can be mixed with suitable additives, such as excipients, stabilizers or inert diluents, and brought by means of the customary methods into the suitable administration forms, such as tablets, coated tablets, hard capsules, 30 aqueous, alcoholic, or oily solutions. Examples of suitable inert carriers are gum arabic, magnesia, magnesium carbonate, potassium phosphate, lactose, glucose, or starch, in particular, corn starch. In this case, the preparation can be carried out both as dry and as moist granules. Suitable oily excipients or solvents are vegetable or animal oils, such as sunflower oil or cod liver oil. Suitable solvents for aqueous or alcoholic solutions are water, ethanol, sugar solutions, or mixtures thereof. 35 Polyethylene glycols and polypropylene glycols are also useful as further auxiliaries for other administration forms. As immediate release tablets, these compositions may contain microcrystalline cellulose, dicalcium phosphate, starch, magnesium stearate and lactose and/or other excipients, binders, extenders, disintegrants, diluents and lubricants known in the art.

When administered by nasal aerosol or inhalation, these compositions may be prepared according to techniques well-known in the art of pharmaceutical formulation and may be prepared as solutions in saline, employing benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, fluorocarbons, and/or other solubilizing or dispersing agents known in the art. Suitable pharmaceutical formulations for administration in the form of aerosols or sprays are, for example, solutions, suspensions or emulsions of the compounds of the invention or their physiologically tolerable salts in a pharmaceutically acceptable solvent, such as ethanol or water, or a mixture of such solvents. If required, the formulation can also additionally contain other pharmaceutical auxiliaries such as surfactants, emulsifiers and stabilizers as well as a propellant.

- 10 For subcutaneous or intravenous administration, the compound according to the invention, if desired with the substances customary therefore such as solubilizers, emulsifiers or further auxiliaries are brought into solution, suspension, or emulsion. The compounds of the invention can also be lyophilized and the lyophilizates obtained used, for example, for the production of injection or infusion preparations. Suitable solvents are, for example, water, physiological saline solution or
- 15 alcohols, e.g. ethanol, propanol, glycerol, in addition also sugar solutions such as glucose or mannitol solutions, or alternatively mixtures of the various solvents mentioned. The injectable solutions or suspensions may be formulated according to known art, using suitable non-toxic, parenterally-acceptable diluents or solvents, such as mannitol, 1,3-butanediol, water, Ringer's solution or isotonic sodium chloride solution, or suitable dispersing or wetting and suspending
- 20 agents, such as sterile, bland, fixed oils, including synthetic mono- or diglycerides, and fatty acids, including oleic acid.

When rectally administered in the form of suppositories, these formulations may be prepared by mixing the compounds according to the invention with a suitable non-irritating excipient, such as cocoa butter, synthetic glyceride esters or polyethylene glycols, which are solid at ordinary

25 temperatures, but liquefy and/or dissolve in the rectal cavity to release the drug.

The compositions can be of value in the veterinary field, which for the purposes herein not only includes the prevention and/or treatment of diseases in animals, but also – for economically important animals such as cattle, pigs, sheep, chicken, fish, etc. – enhancing the growth and/or weight of the animal and/or the amount and/or the quality of the meat or other products obtained

30 from the animal. Thus, in a further aspect, the invention relates to a (pharmaceutical) composition for veterinary use that contains at least one compound of the invention and at least one suitable carrier (i.e. a carrier suitable for veterinary use). The invention also relates to the use of a compound of the invention in the preparation of such a composition.

Examples

- 35 The following examples are provided for the purpose of illustrating the present invention and by no means should be interpreted to limit the scope of the present invention.

Example 1. Synthesis of the compounds of the invention

All reagents used were purchased from chemical suppliers and used without purification. Thin-layer chromatography (TLC) was performed using silica gel 60 F254 plates, with observation under UV when necessary.

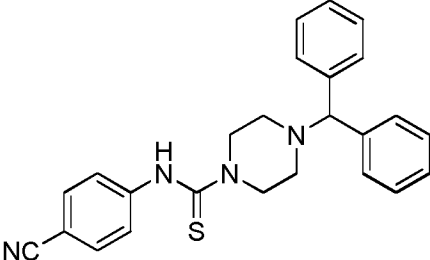
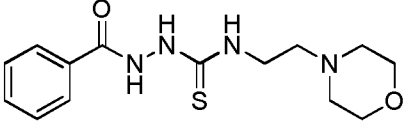
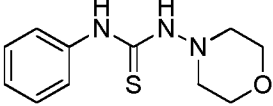
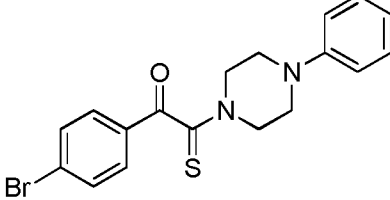
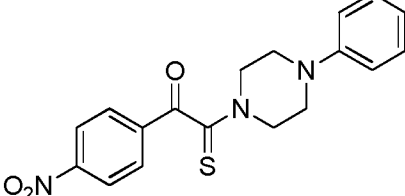
5 Melting points were recorded on an Electrothermal IA9000 melting point system.

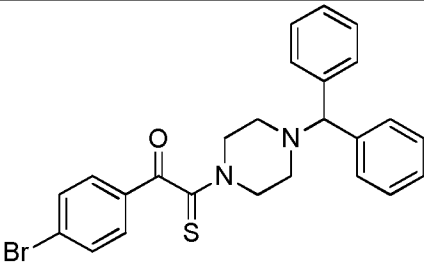
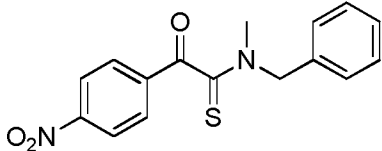
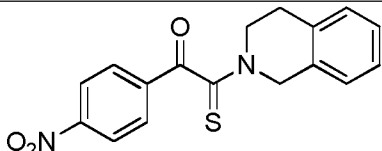
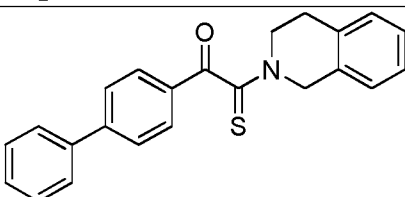
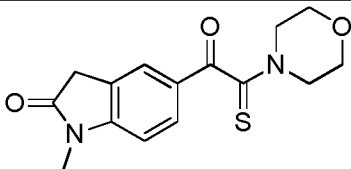
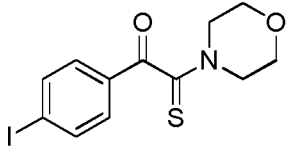
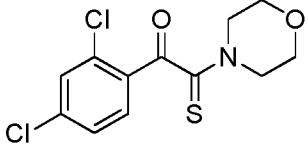
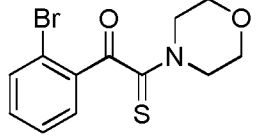
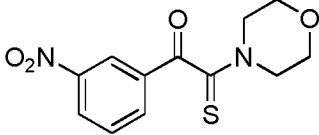
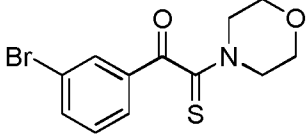
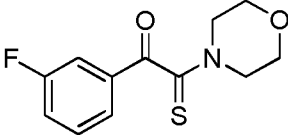
^1H NMR spectra were recorded on an AVANCE II 400 MHz Bruker spectrometer with CDCl_3 or $\text{DMSO-}d_6$ as the solvent. ^{13}C NMR spectra were recorded at 100 MHz. All coupling constants were measured in hertz (Hz), and the chemical shifts (δ_{H} and δ_{C}) were quoted in parts per million (ppm) relative to TMS (δ_0), which was used as the internal standard. Data were reported as follows:

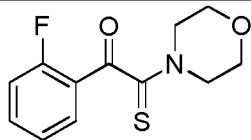
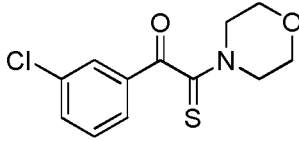
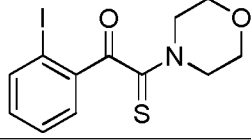
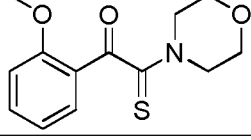
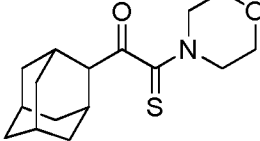
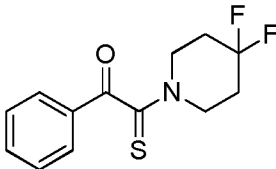
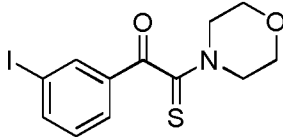
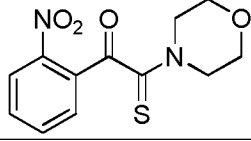
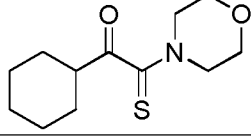
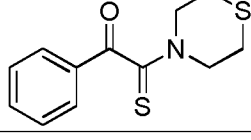
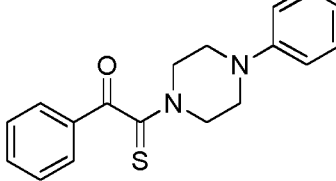
10 chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), integration, and coupling constant (Hz). High-resolution mass spectroscopy was carried out on an LTQ-Orbitrap XL hybrid system.

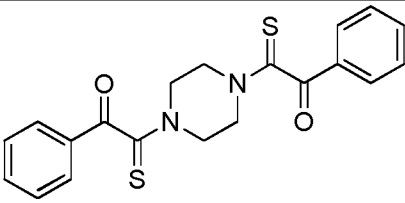
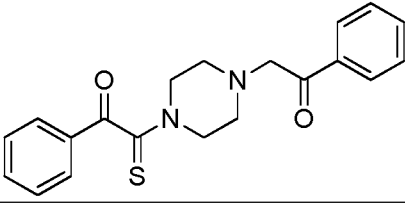
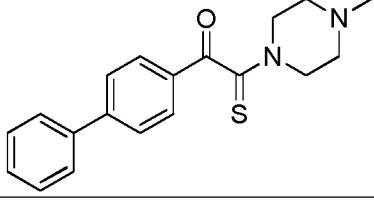
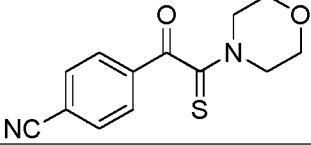
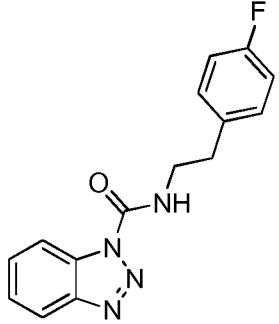
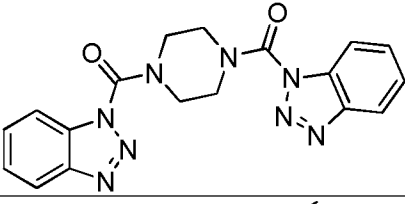
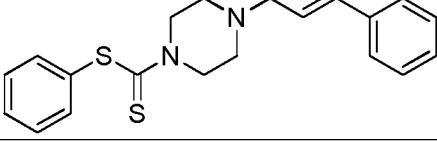
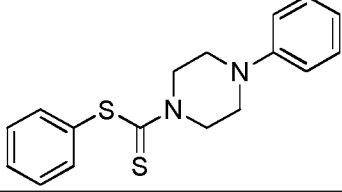
Exemplary compounds of the present invention are shown in table 1.

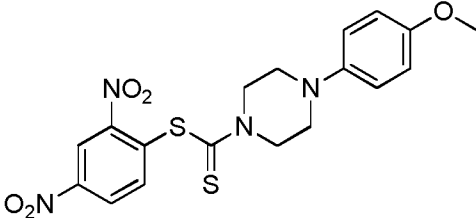
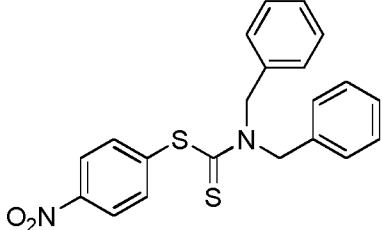
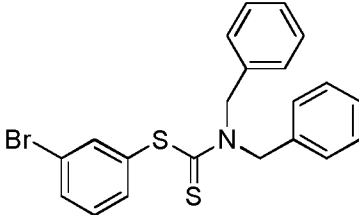
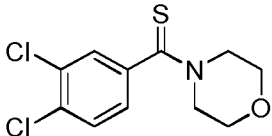
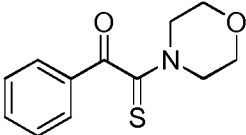
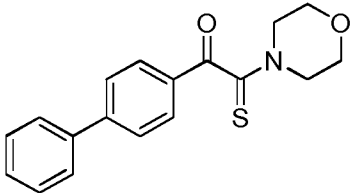
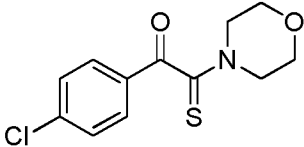
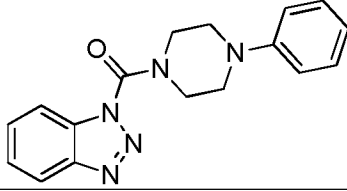
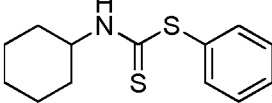
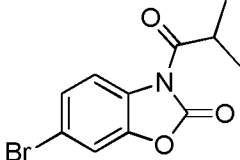
Table 1

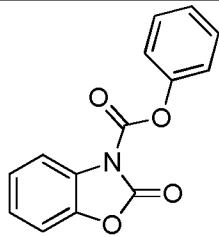
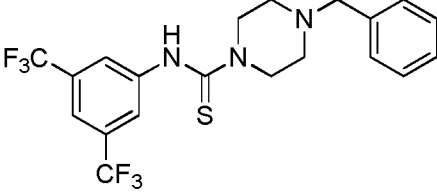
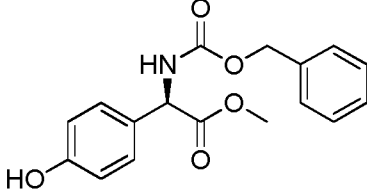
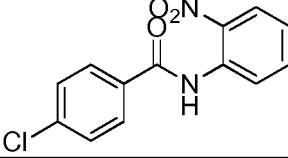
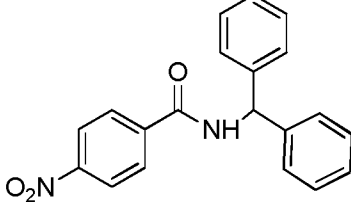
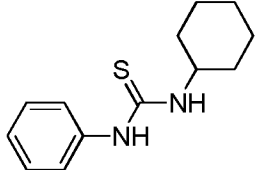
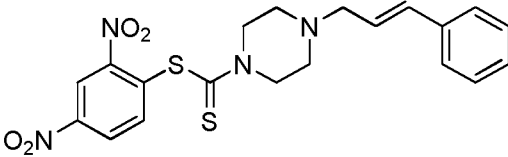
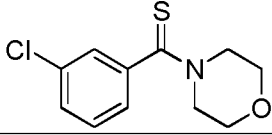
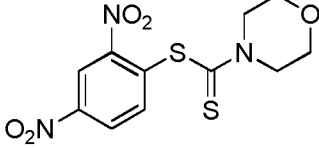
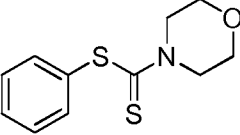
Compound number	Structure	CAS n°
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2		-
3		-
4		-
5		-

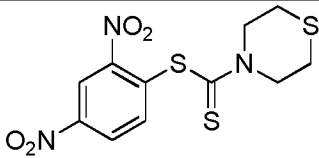
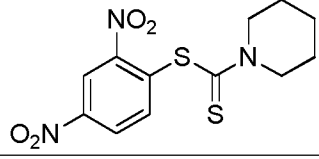
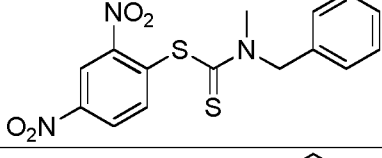
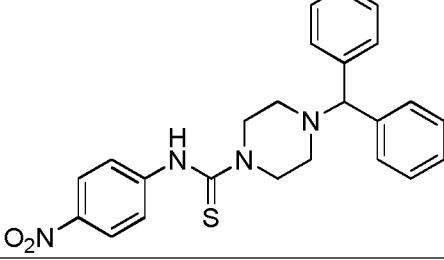
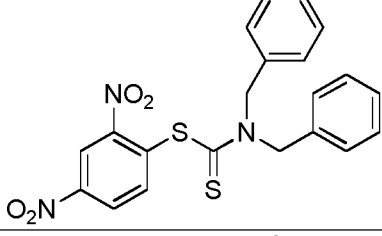
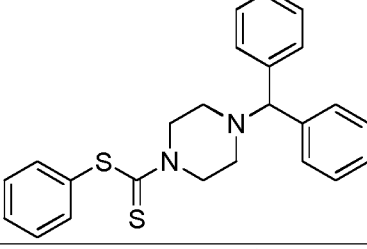
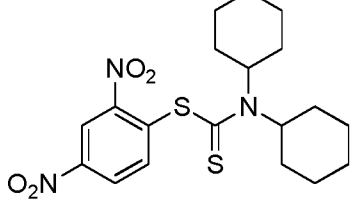
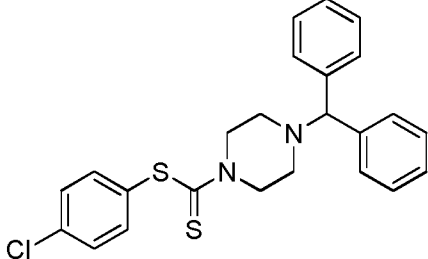
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16		-

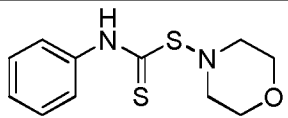
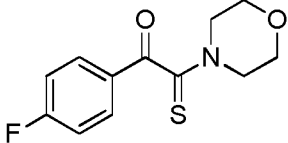
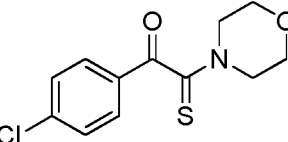
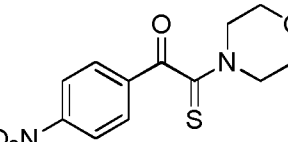
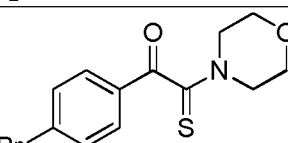
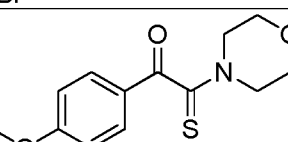
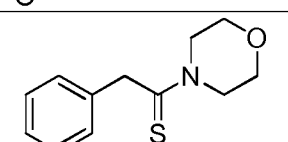
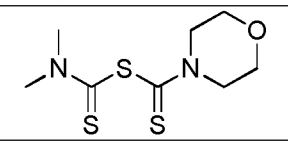
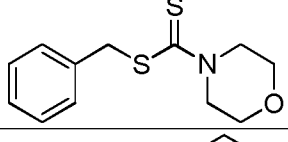
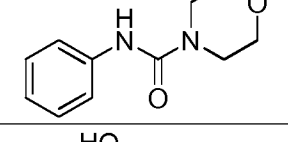
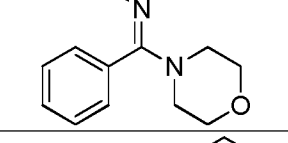
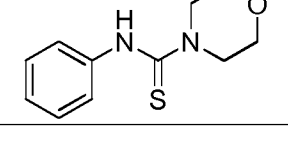
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18	 <chem>O=C(SN1CCOCC1)c2cccc(c2)Cl</chem>	-
19	 <chem>O=C(SN1CCOCC1)c2cccc(c2)I</chem>	-
20	 <chem>COc1cccc(c1)C(=O)SNC2CCOCC2</chem>	-
21	 <chem>O=C(SN1CCOCC1)C23CC4CC1CC2CC3C4</chem>	-
22	 <chem>O=C(SN1CC(F)(F)CC1)c2ccccc2</chem>	-
23	 <chem>O=C(SN1CCOCC1)c2cccc(c2)I</chem>	-
24	 <chem>O=C(SN1CCOCC1)c2cccc(c2)[N+](=O)[O-]</chem>	-
25	 <chem>O=C(SN1CCOCC1)C2CCCCC2</chem>	-
26	 <chem>O=C(SN1CCSCC1)c2ccccc2</chem>	-
27	 <chem>O=C(SN(C)CNc1ccccc1)c2ccccc2</chem>	-

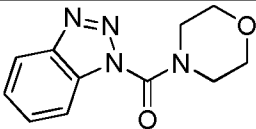
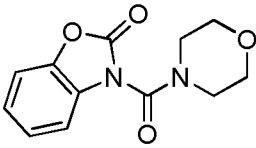
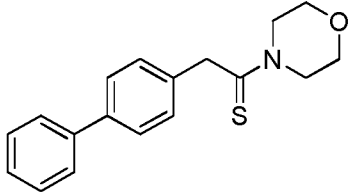
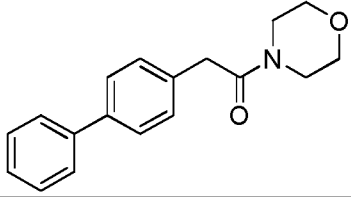
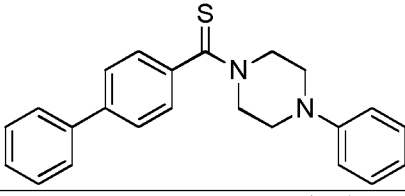
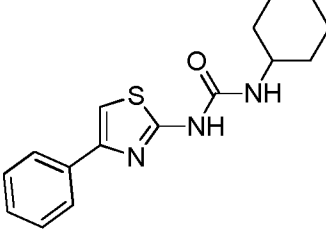
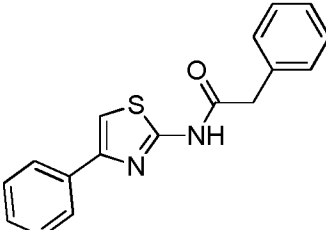
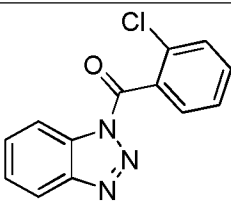
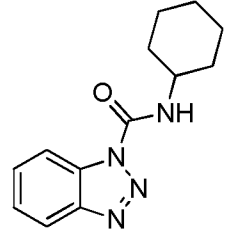
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35		-

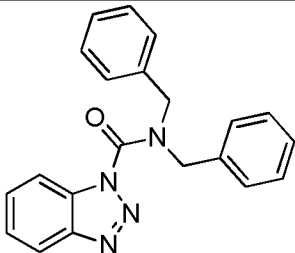
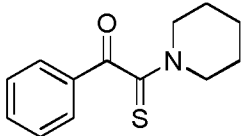
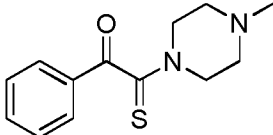
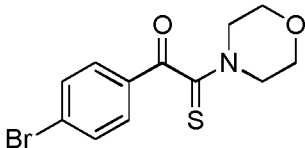
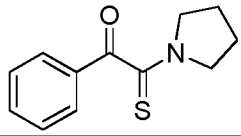
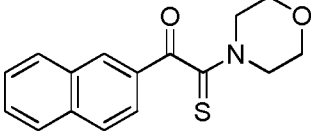
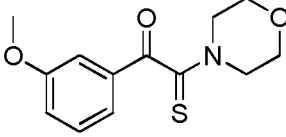
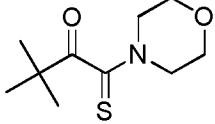
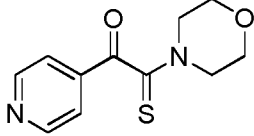
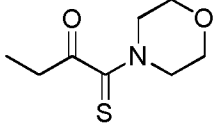
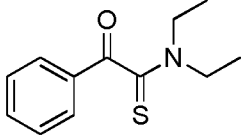
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37		-
38		-
39		675845-03-1
40		5509-99-9
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43		1233852-29-3
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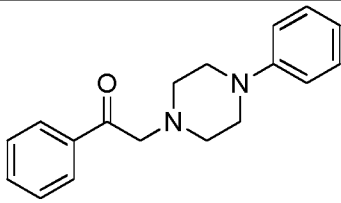
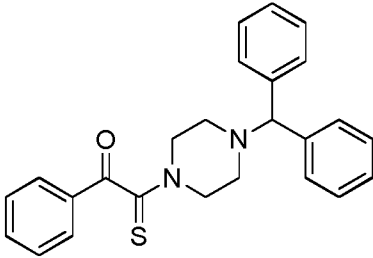
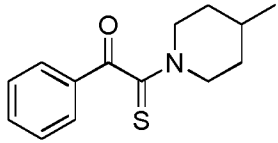
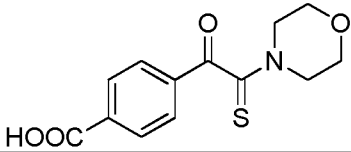
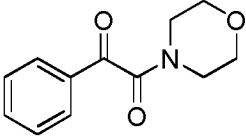
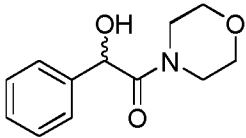
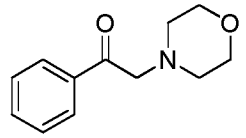
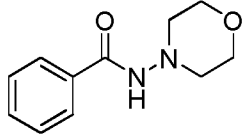
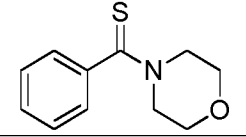
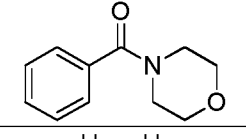
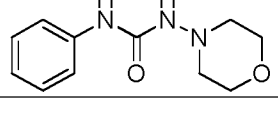
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49		33489-99-5
50		88229-34-9
51		102-08-9
52		1381994-30-4
53		76226-60-3
54		16913-59-0
55		16913-58-9

56		1381994-24-6
57		897-73-4
58		1381994-26-8
59		405067-49-4
60		25675-99-4
61		1381994-11-1
62		16913-54-5
63		1381994-13-3

64		24171-18-4
65		1613631-62-1
66		57495-15-5
67		92848-73-2
68		13621-46-0
69		100372-92-7
70		949-01-9
71		30887-90-2
72		28249-25-4
73		4559-92-6
74		65623-52-1
75		15093-54-6

76		190511-45-6
77		302782-79-2
78		5428-57-9
79		86540-07-0
80		933671-45-5
81		221389-37-3
82		205928-24-1
83		30457-12-6
84		70243-23-1

85		190511-52-5
86		58861-75-9
87		1613631-59-6
88		13621-46-0
89		1428263-66-4
90		1033590-39-4
91		1447938-97-7
92		220102-35-2
93		1033590-37-2
94		90087-83-5
95		128592-68-7

96	 <chem>O=C(CN1CCN(C1)Cc2ccccc2)c3ccccc3</chem>	97888-63-6
97	 <chem>O=C(SN1CCN(C1)C(c2ccccc2)c3ccccc3)c4ccccc4</chem>	1381994-09-7
98	 <chem>O=C(SN1CC(C)CC1)c2ccccc2</chem>	1391504-90-7
99	 <chem>O=C(SN1CCOCC1)c2cc(ccc2C(=O)O)C(=O)N</chem>	1033590-40-7
100	 <chem>O=C(N1CCOCC1)c2ccccc2C(=O)N</chem>	40991-78-4
101	 <chem>O=C(N1CCOCC1)[C@H](O)c2ccccc2</chem>	57872-39-6
102	 <chem>O=C(CN1CCOCC1)c2ccccc2</chem>	779-53-3
103	 <chem>O=C(N1CCOCC1)c2ccccc2</chem>	5454-04-6
104	 <chem>O=C(SN1CCOCC1)c2ccccc2</chem>	2032-36-2
105	 <chem>O=C(N1CCOCC1)c2ccccc2</chem>	1468-28-6
106	 <chem>O=C(N1CCOCC1)Nc2ccccc2</chem>	13262-39-0

Compound 1. *4-benzhydryl-N-(4-cyanophenyl)piperazine-1-carbothioamide*. To a solution of 4-cyanophenyl isothiocyanate (0.50 g, 3.12 mmol) in methanol was added 1-(diphenylmethyl)piperazine (0.94 g, 3.74 mmol). The mixture was stirred for 3h at room temperature and the reaction monitored by TLC. After completion of the reaction, the precipitate was filtered off and purified by column chromatography (hexane/EtOAc, 8:2) to yield the target compound as white solid (1.08 g, 84%). Mp: 147-149°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 2.48-2.50 (m, 4H), 3.75 - 3.77 (m, 4H), 4.33 (s, 1H), 7.08-7.18 (m, 4 ArH), 7.19-7.25 (m, 4 ArH), 7.30-7.35 (m, 4 ArH), 7.49-7.53 (m, 2 ArH).

Compound 2. *2-benzoyl-N-(2-morpholinoethyl)hydrazinecarbothioamide*. Benzoylhydrazine (1.00 g, 7.34 mmol) was diluted in 20 ml of MeOH (25mL) and, after complete dissolution, 4-(2-isothiocyanatoethyl)morpholine (1.17 g, 7.34 mmol) was added dropwise to the solution and stirred 2h with apparition of white solid. The reaction was followed by TLC and after complete transformation of the starting material, the mixture was evaporated and the product was recrystallized in MeOH (white crystal, 1.65 g, 73%). R_f 0.5 (EtOAc/EtOH 3:2). Mp: 140-142°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 2.60 (m, 6H), 3.68 (m, 6H), 7.49 (dd, 2 ArH, J = 7.4 Hz), 7.59 (m, 1 ArH), 7.89 (dd, 2 ArH, J = 7.5 Hz). ¹³C NMR (100 MHz, CDCl₃): δ_C (ppm) 50.97 (2C), 54.16 (2C), 63.94, 97.38, 125.48 (2C), 126.08 (2C), 129.81, 158.43 (C=O), 167.70 (C=S).

Compound 3. *1-morpholino-3-phenylthiourea*. To a solution of isothiocyanatobenzene (1.00 g, 7.40 mmol) in MeOH, 4-amino-morpholin (0.91 g, 8.90 mmol) was slowly added and the reaction was monitored with TLC until complete disappearance of the starting material. A white solid was appeared in the mixture (3 hrs). The solution was then filtered and the white solid recovered was recrystallized in MeOH to afford the desired product (white crystal, 1.40 g, 80%). R_f 0.4 (EtOAc/Cyclohexane 2:3). Mp: 160-162°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 2.77 (t, 2H, J = 4.3 Hz), 3.05 (t, 2H, J = 4.3 Hz), 3.69 (m, 2H), 3.94 (m, 2H), 7.10 (br s, 1 NH), 7.23 (m, 1 ArH), 7.39 (dd, 2 ArH, J = 7.5 Hz), 7.60 (dd, 2 ArH, J = 7.4 Hz), 9.12 (br s, 1 NH). ¹³C NMR (100 MHz, CDCl₃): δ_C (ppm) 53.80 (2C), 64.58 (2C), 122.46 (2C), 124.28, 126.71 (2C), 176.72 (C=S).

General procedure I. To a stirred solution of ketone derivative (1 eq) in chloroform was added dropwise a solution of dibromine (1.2 eq) in chloroform. After 2 hours, the solvent was evaporated *in vacuo* to give a crude oil consisting mainly of 2-bromo-1-(substituted)-ethanone compound along with trace amounts of 2,2-dibromo-1-(substituted)-ethanone compound. The mixture was used without purification in the next step. To the commercial or synthesized 2-bromo-1-(substituted)-ethanone derivative were added in sequence DMF, cyclooctasulfur (1.5 eq) and morpholine (3 eq). The mixture was then stirred at room temperature. After completion of the reaction, the reaction mixture was quenched with distilled water to give a precipitate which was further washed with distilled water.

Compound 4. *1-(4-bromophenyl)-2-(4-phenylpiperazin-1-yl)-2-thioxoethanone*. This compound was synthesized according to the general procedure I using commercial 2-bromo-1-(4-bromophenyl)-ethanone (1.00 g, 3.62 mmol), 1-phenylpiperazine (1.65 mL, 10.87 mmol) and sulfur (0.17 g, 5.43

mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a colorless solid (0.60 g, 43%). Mp: 124-125°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.10-3.12 (t, 2H, J = 4.8 Hz), 3.28-3.30 (t, 2H, J = 4.8 Hz), 3.77-3.79 (t, 2H, J = 4.8 Hz), 3.39-3.41 (t, 2H, J = 4.8 Hz), 6.80-6.92 (m, 3 ArH), 7.20-7.29 (m, 2H), 7.60 (d, 2H, J = 8.0 Hz), 7.80 (d, 2H, J = 8.0 Hz).

- 5 **Compound 5.** *1-(4-nitrophenyl)-2-(4-phenylpiperazin-1-yl)-2-thioxoethanone*. This compound was synthesized according to the general procedure I using commercial 2-bromo-1-(4-nitrophenyl)-ethanone (1.50 g, 6.17 mmol), 1-phenylpiperazine (2.80 mL, 18.52 mmol) and sulfur (0.29 g, 9.26 mmol) in DMF (10 mL). Ethanol was used for recrystallization to afford the title compound as a yellow solid (0.83 g, 38%). Mp: 138-140°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.11-3.14 (t, 2H, J = 4.8 Hz), 3.38-3.40 (t, 2H, J = 4.8 Hz), 3.71-3.73 (t, 2H, J = 4.8 Hz), 4.48-4.50 (t, 2H, J = 4.8 Hz), 6.80-6.89 (m, 3 ArH), 7.24-7.28 (m, 2H), 8.25 (d, 2H, J = 8.0 Hz), 8.51 (d, 2H, J = 8.0 Hz).

- Compound 6.** *2-(4-benzhydrylpiperazin-1-yl)-1-(4-bromophenyl)-2-thioxoethanone*. This compound was synthesized according to the general procedure I using commercial 2-bromo-1-(4-bromophenyl)-ethanone (1.00 g, 3.62 mmol), 1-(diphenylmethyl)piperazine (2.73 g, 10.87 mmol) and sulfur (0.17 g, 5.43 mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a colorless solid (0.81 g, 47%). Mp: 128-130°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 2.38 (br s, 2H), 2.55-2.57 (t, 2H, J = 4.8 Hz), 3.50-3.52 (t, 2H, J = 4.8 Hz), 4.25 (br s, 2H), 7.1-7.16 (m, 2 ArH), 7.19-7.24 (m, 4 ArH), 7.30-7.35 (m, 4 ArH), 7.51-7.58 (m, 2 ArH), 7.73-7.78 (m, 2 ArH).

- Compound 7.** *N-benzyl-N-methyl-2-(4-nitrophenyl)-2-oxoethanethioamide*. This compound was synthesized according to the general procedure I using commercial 2-bromo-1-(4-nitrophenyl)-ethanone (1.50 g, 6.17 mmol), *N*-methylbenzylamine (2.38 mL, 18.52 mmol) and sulfur (0.29 g, 9.26 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) to give the title compound as yellow oil (0.46 g, 24%). Mp: 108-110°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.08 (s, 3H), 5.20 (s, 2H), 7.31-7.40 (m, 5 ArH), 8.12 (d, 2H, J = 8.0 Hz), 8.51 (d, 2H, J = 8.0 Hz).

- Compound 8.** *2-(3,4-dihydroisoquinolin-2(1H)-yl)-1-(4-nitrophenyl)-2-thioxoethanone*. This compound was synthesized according to the general procedure I using commercial 2-bromo-1-(4-nitrophenyl)-ethanone (1.50 g, 6.17 mmol), 1,2,3,4-tetrahydroisoquinoline (2.32 mL, 18.52 mmol) and sulfur (0.29 g, 9.26 mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a yellow solid (0.92 g, 46%). Mp: 140-142°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 2.95-2.98 (t, 2H, J = 4.8 Hz), 3.80-3.82 (t, 2H, J = 4.8 Hz), 5.38 (s, 2H), 7.10-7.26 (m, 4 ArH), 8.14 (d, 2H, J = 8.0 Hz), 8.52 (d, 2H, J = 8.0 Hz).

- Compound 9.** *1-([1,1'-biphenyl]-4-yl)-2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-thioxoethanone*. This compound was synthesized according to the general procedure I using commercial 1-([1,1'-biphenyl]-4-yl)-2-bromoethanone (1.00 g, 3.64 mmol), 1,2,3,4-tetrahydroisoquinoline (1.37 mL, 10.94 mmol) and sulfur (0.17 g, 5.46 mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a yellow solid (0.51 g, 39%). Mp: 129-131°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 2.95-2.98 (t, 2H, J = 4.8 Hz), 3.85-3.87 (t, 2H, J = 4.8 Hz), 5.37 (s, 2H), 7.10-7.12

(m, 1 ArH), 7.20-7.23 (m, 2 ArH), 7.30-7.43 (m, 4 ArH), 7.53-7.58 (m, 2 ArH), 7.62 (d, 2H, $J = 8.0$ Hz), 8.02 (d, 2H, $J = 8.0$ Hz).

Compound 10. *1-methyl-5-(2-morpholino-2-thioxoacetyl)indolin-2-one*. This compound was synthesized according to the general procedure I. 5-Acetyl-1-methylindolin-2-one (1.00 g, 5.28 mmol) and dibromine (0.32 mL, 6.34 mmol) were mixed in chloroform (15 mL) to obtain the 5-(2-bromoacetyl)-1-methylindolin-2-one and this intermediate was reacted in a second time with morpholine (1.39 mL, 15.84 mmol) and sulfur (0.25 g, 7.92 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) and the obtained oil was collected by filtration with diethyl ether to give the title compound as a yellow solid (0.29 g, 18%). Mp: 216-218°C.

¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 2.10 (s, 2H), 3.42 (s, 3H), 3.50-3.52 (t, 2H, $J = 4.8$ Hz), 3.60-3.62 (t, 2H, $J = 4.8$ Hz), 3.85-3.88 (t, 2H, $J = 4.8$ Hz), 4.29-4.31 (t, 2H, $J = 4.8$ Hz), 6.98 (d, 2 ArH, $J = 8.2$ Hz), 7.78 (d, 1 ArH, $J = 1.1$ Hz), 7.82 (dd, 1 ArH, $J = 1.1$ and 8.2 Hz).

Compound 11. *1-(4-iodophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 1-(4-Iodophenyl)ethanone (1.00 g, 4.00 mmol) and dibromine (0.24 mL, 4.87 mmol) were mixed in chloroform (15 mL) to obtain the 2-bromo-1-(2-iodophenyl)-ethanone and this intermediate was reacted in a second time with morpholine (1.06 mL, 12.20 mmol) and sulfur (0.19 g, 6.10 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) to give the title compound as a yellow oil (0.35 g, 24%). R_f 0.3 (cyclohexane/EtOAc 8:2). Mp: 175-177°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.50-3.52 (t, 2H, $J = 4.8$ Hz), 3.59-3.61 (t, 2H, $J = 4.8$ Hz), 3.78-3.80 (t, 2H, $J = 4.8$ Hz), 4.25-4.27 (t, 2H, $J = 4.8$ Hz), 7.63 (d, 2H, $J = 8.2$ Hz), 7.80 (d, 2H, $J = 8.2$ Hz).

Compound 12. *1-(2,4-dichlorophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-(2,4-dichlorophenyl)-ethanone (1.00 g, 3.76 mmol), morpholine (0.99 mL, 11.28 mmol) and sulfur (0.18 g, 5.64 mmol) in DMF (10 mL). Acetonitrile was used for recrystallization to afford the title compound as a yellow solid (0.31 g, 28%). R_f 0.4 (cyclohexane/EtOAc 8:2). Mp: 116-118°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.75-3.77 (t, 2H, $J = 4.8$ Hz), 3.77-3.79 (t, 2H, $J = 4.8$ Hz), 3.89-3.91 (t, 2H, $J = 4.8$ Hz), 4.10-4.12 (t, 2H, $J = 4.8$ Hz), 7.30 (dd, 1 ArH, $J = 2.6$ and 8.4 Hz), 7.38 (d, 1 ArH, $J = 2.6$ Hz), 7.80 (d, 1 ArH, $J = 8.4$ Hz).

Compound 13. *1-(2-bromophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-(2-bromophenyl)-ethanone (0.50 g, 1.81 mmol), morpholine (0.48 mL, 5.43 mmol) and sulfur (0.08 g, 2.72 mmol) in DMF (10 mL). Ethanol was used for recrystallization to afford the title compound as a colorless solid (0.28 g, 52%). R_f 0.3 (cyclohexane/EtOAc 8:2). Mp: 81-83°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.48-3.85 (m, 4H), 3.90-3.92 (t, 2H, $J = 4.8$ Hz), 4.25-4.28 (t, 2H, $J = 4.8$ Hz), 7.27-7.40 (ddd, 1 ArH, $J = 1.8$ and 7.8 Hz), 7.40-7.46 (ddd, 1 ArH, $J = 1.2$ and 7.5 Hz), 7.59-7.62 (dd, 1 ArH, $J = 1.1$ and 7.9 Hz), 7.84-7.87 (dd, 1 ArH, $J = 1.8$ and 7.6 Hz).

Compound 14. *1-(3-Nitrophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using commercial 2-bromo-1-(3-nitrophenyl)-ethanone (1.50 g, 6.17 mmol), morpholine (1.61 mL, 18.52 mmol) and sulfur (0.29 g, 9.26 mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a colorless solid (1.26 g, 73%). R_f 0.1 (cyclohexane/EtOAc 8:2). Mp: 179-181°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.58-3.60 (t, 2H, $J = 4.8$ Hz), 3.67-3.69 (t, 2H, $J = 4.8$ Hz), 3.86-3.89 (t, 2H, $J = 4.8$ Hz), 4.28-4.30 (t, 2H, $J = 4.8$ Hz), 7.63-7.67 (DD, 1 ArH, $J = 8.6$ Hz), 8.26-8.29 (m, 1 ArH), 8.38-8.40 (m, 1 ArH), 8.73-8.74 (dd, 1 ArH, $J = 1.9$ Hz). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 47.42, 52.12, 66.41, 66.57, 124.56, 128.36, 130.20, 135.18, 148.51, 184.29 (C=O), 193.48 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$ (M + H) $^+$ 281.0590, found 281.0588.

Compound 15. *1-(3-Bromophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-(3-bromophenyl)-ethanone (0.50 g, 1.81 mmol), morpholine (0.48 mL, 5.43 mmol) and sulfur (0.08 g, 2.72 mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a colorless solid (0.14 g, 26%). R_f 0.2 (cyclohexane/EtOAc 8:2). Mp: 104-106°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.61-3.64 (t, 2H, $J = 4.8$ Hz), 3.72-3.74 (t, 2H, $J = 4.8$ Hz), 3.90-3.93 (t, 2H, $J = 4.8$ Hz), 4.33-4.35 (t, 2H, $J = 4.8$ Hz), 7.36-7.40 (m, 1 ArH), 7.73-7.75 (m, 1 ArH), 7.90-7.92 (m, 1 ArH), 8.13-8.15 (m, 1 ArH). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 44.79, 49.58, 63.97, 64.11, 120.80, 126.03, 128.08, 130.10, 132.81, 134.81, 183.54 (C=O), 192.09 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{12}\text{H}_{12}\text{BrNO}_2\text{S}$ (M + H) $^+$ 313.9844, found 313.9844.

Compound 16. *1-(3-Fluorophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-(3-fluorophenyl)ethanone (0.50 g, 2.30 mmol), morpholine (0.6 mL, 6.90 mmol) and sulfur (0.11 g, 3.45 mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a yellow solid (0.13 g, 23%). R_f 0.2 (cyclohexane/EtOAc 8:2). Mp: 95-97°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.59-3.62 (t, 2H, $J = 4.8$ Hz), 3.70-3.73 (t, 2H, $J = 4.8$ Hz), 3.90-3.93 (t, 2H, $J = 4.8$ Hz), 4.32-4.34 (t, 2H, $J = 4.8$ Hz), 7.30-7.35 (DDdd, 1 ArH, $J_{\text{HF}} = 16.4$ Hz $J_{\text{HH}} = 8.1$ and 2.5 Hz), 7.46-7.51 (DDd, 1 ArH, $J_{\text{HH}} = 8.1$ Hz $J_{\text{HF}} = 5.4$ Hz), 7.68-7.72 (Ddd, 1 ArH, $J_{\text{HF}} = 9.0$ Hz $J_{\text{HH}} = 1.6$ Hz), 7.76-7.78 (Ddd, 1 ArH, $J_{\text{HH}} = 7.7$ Hz and 1.1 Hz). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 45.37, 50.17, 64.57, 64.70, 114.39 (d, $J_{\text{CF}} = 23$ Hz), 119.62 (d, $J_{\text{CF}} = 23$ Hz), 123.89 (d, $J_{\text{CF}} = 23$ Hz), 128.86 (d, $J_{\text{CF}} = 23$ Hz), 133.66 (d, $J_{\text{CF}} = 23$ Hz), 159.78 (D, $J_{\text{CF}} = 247$ Hz), 184.40 (C=O), 192.97 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{12}\text{H}_{12}\text{FNO}_2\text{S}$ (M + H) $^+$ 254.0645, found 254.0644.

Compound 17. *1-(2-Fluorophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 1-(2-Fluorophenyl)ethanone (1.50 g, 11.10 mmol) and dibromine (0.65 mL, 13.00 mmol) were mixed in chloroform (15 mL) to obtain the 2-bromo-1-(2-fluorophenyl)-ethanone and this intermediate was reacted in a second time with morpholine (2.84 mL, 32.50 mmol) and sulfur (0.52 g, 16.20 mmol) in DMF (10 mL). Methanol was used for recrystallization to afford the title compound as a yellow solid (1.09 g, 39%). R_f 0.2

(cyclohexane/EtOAc 8:2). Mp: 83-85°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.71-3.73 (t, 2H, *J* = 4.8 Hz), 3.78-3.81 (t, 2H, *J* = 4.8 Hz), 3.90-3.92 (t, 2H, *J* = 4.8 Hz), 4.26-4.28 (t, 2H, *J* = 4.8 Hz), 7.10-7.16 (Ddd, 1 ArH, *J*_{HF} = 10.9 Hz *J*_{HH} = 8.3 and 1.0 Hz), 7.29-7.33 (DDd, 1 ArH, *J*_{HH} = 7.8 and 1.0 Hz), 7.59-7.61 (m, 1 ArH), 8.00-8.05 (Ddd, 1 ArH, *J*_{HF} = 15.2 Hz *J*_{HH} = 7.6 and 1.9 Hz). ¹³C NMR (100 MHz, CDCl₃): δ_C (ppm) 44.97, 49.65, 63.86, 63.87, 114.30 (d, *J*_{CF} = 22 Hz), 120.91 (d, *J*_{CF} = 23 Hz), 122.74 (d, *J*_{CF} = 23 Hz), 129.49 (d, *J*_{CF} = 23 Hz), 133.76 (d, *J*_{CF} = 23 Hz), 158.06 (D, *J*_{CF} = 255 Hz), 181.35 (C=O), 194.23 (C=S). HRMS (ESI⁺): *m/z* calcd for C₁₂H₁₂FNO₂S (M + H)⁺ 254.0645, found 254.0644.

Compound 18. *1-(3-Chlorophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 1-(3-Chlorophenyl)ethanone (2.00 g, 12.90 mmol) and dibromine (0.78 mL, 15.50 mmol) were mixed in chloroform (15 mL) to obtain the 2-bromo-1-(3-chlorophenyl)-ethanone and this intermediate was reacted in a second time with morpholine (3.38 mL, 38.80 mmol) and sulfur (0.62 g, 19.40 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) and the obtained oil was collected by filtration with diethyl ether to give the title compound as a yellow solid (1.50 g, 43%). *R*_f 0.2 (cyclohexane/EtOAc 8:2). Mp: 92-94°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.59-3.61 (t, 2H, *J* = 4.8 Hz), 3.70-3.72 (t, 2H, *J* = 4.8 Hz), 3.90-3.92 (t, 2H, *J* = 4.8 Hz), 4.31-4.33 (t, 2H, *J* = 4.8 Hz), 7.42-7.46 (DD, 1 ArH, *J* = 7.8 Hz), 7.57-7.59 (Ddd, 1 ArH, *J* = 8.0 and 1.0 Hz), 7.85-7.87 (Ddd, 1 ArH, *J* = 7.8 and 1.4 Hz), 7.96-7.97 (dd, 1 ArH, *J* = 1.8 Hz). ¹³C NMR (100 MHz, CDCl₃): δ_C (ppm) 47.21, 52.00, 66.39, 66.52, 127.98, 129.61, 130.28, 134.33, 135.05, 135.30, 186.07 (C=O), 194.60 (C=S). HRMS (ESI⁺): *m/z* calcd for C₁₂H₁₂ClNO₂S (M + H)⁺ 270.0277, found 270.0278.

Compound 19. *1-(2-Iodophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 1-(2-Iodophenyl)ethanone (1.00 g, 4.00 mmol) and dibromine (0.24 mL, 4.87 mmol) were mixed in chloroform (15 mL) to obtain the 2-bromo-1-(2-iodophenyl)-ethanone and this intermediate was reacted in a second time with morpholine (1.06 mL, 12.20 mmol) and sulfur (0.19 g, 6.10 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) to give the title compound as a yellow oil (0.70 g, 47%). *R*_f 0.2 (cyclohexane/EtOAc 8:2). ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 3.80-3.85 (m, 4H), 3.91-3.93 (t, 2H, *J* = 4.8 Hz), 4.27-4.30 (t, 2H, *J* = 4.8 Hz), 7.17-7.21 (DDd, 1 ArH, *J* = 7.5 and 1.5 Hz), 7.43-7.47 (Ddd, 1 ArH, *J* = 7.5 and 1.1 Hz), 7.74-7.77 (Dd, 1 ArH, *J* = 7.8 and 1.5 Hz), 7.97-7.99 (Dd, 1 ArH, *J* = 7.9 and 1.1 Hz). ¹³C NMR (100 MHz, CDCl₃): δ_C (ppm) 46.93, 51.46, 65.19, 65.28, 92.48, 127.22, 131.65, 132.62, 137.25, 140.64, 185.16 (C=O), 193.15 (C=S). HRMS (ESI⁺): *m/z* calcd for C₁₂H₁₂INO₂S (M + H)⁺ 361.9706, found 361.9706.

Compound 20. *1-(2-Methoxyphenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 1-(2-Methoxyphenyl)ethanone (2.00 g, 13.30 mmol) and dibromine (0.81 mL, 16.00 mmol) were mixed in chloroform (15 mL) to obtain the 2-bromo-1-(2-methoxyphenyl)-ethanone and this intermediate was reacted in a second time with morpholine (3.48 mL, 40.00 mmol) and sulfur (0.64 g, 20.00 mmol) in DMF (10 mL). Cyclohexane

was used for recrystallization to afford the title compound as a yellow solid (1.76 g, 50%). R_f 0.2 (cyclohexane/EtOAc 8:2). Mp: 158-160°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.67-3.68 (t, 2H, $J = 4.8$ Hz), 3.76-3.78 (t, 2H, $J = 4.8$ Hz), 3.88-3.90 (t, 2H, $J = 4.8$ Hz), 4.24-4.27 (t, 2H, $J = 4.8$ Hz), 6.97-6.99 (D, 1 ArH, $J = 8.4$ Hz), 7.08-7.11 (DD, 1 ArH, $J = 7.4$ Hz), 7.53-7.58 (DDd, 1 ArH, $J = 7.9$ and 1.7 Hz), 7.97-8.00 (Dd, 1 ArH, $J = 7.8$ and 1.7 Hz). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 47.99, 51.71, 56.37, 66.25, 112.55, 121.54, 124.34, 131.82, 135.58, 159.15, 186.62 (C=O), 198.31 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_3\text{S}$ (M + H) $^+$ 266.0845, found 266.0847.

Compound 21. *1-((1*r*,3*r*,5*r*,7*r*)Adamantan-2-yl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-((1*r*,3*r*,5*r*,7*r*)adamantan-2-yl)-ethanone (1 g, 3.90 mmol), morpholine (1.02 mL, 11.70 mmol) and sulfur (0.18 g, 5.90 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) to give the title compound as a yellow oil (0.08 g, 8%). R_f 0.3 (hexane/EtOAc 8:2). ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 1.69-1.77 (m, 6H), 2.02-2.05 (m, 9H), 3.51 (m, 2H), 3.73-3.75 (t, 2H, $J = 4.8$ Hz), 3.80-3.83 (t, 2H, $J = 4.8$ Hz), 4.18 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 27.96 (3C), 36.30 (3C), 39.79 (3C), 45.03, 46.41, 52.39, 66.30, 66.36, 196.66 (C=O), 205.54 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{16}\text{H}_{23}\text{NO}_2\text{S}$ (M + H) $^+$ 294.1522, found 294.1523.

Compound 22. *1-Phenyl-2-(4,4-difluoropiperidin-1-yl)-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-phenylethanone (0.50 g, 2.52 mmol), 4,4-difluoropiperidine hydrochloride (1.19 g, 7.56 mmol), triethylamine (1.05 mL, 7.56 mmol) and sulfur (0.12 g, 3.78 mmol) in DMF (10 mL). Cyclohexane was used for recrystallization to afford the title compound as a colorless solid (0.12 g, 18%). R_f 0.5 (cyclohexane/EtOAc 8:2). Mp: 119-121°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 1.42-2.25 (m, 4H), 3.64-3.68 (m, 2H), 4.42-4.46 (m, 2H), 7.48-7.52 (m, 2 ArH), 7.61-7.65 (m, 1 ArH), 7.98-8.00 (m, 2 ArH). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 31.49 (t, $J_{\text{CF}} = 24$ Hz), 32.56 (t, $J_{\text{CF}} = 24$ Hz), 41.78 (t, $J_{\text{CF}} = 6$ Hz), 46.28 (t, $J_{\text{CF}} = 6$ Hz), 118.84 (D, $J_{\text{CF}} = 242$ Hz), 127.18 (2C), 128.02 (2C), 131.23, 132.77, 186.10 (C=O), 194.87 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{13}\text{H}_{13}\text{F}_2\text{NOS}$ (M + H) $^+$ 270.0758, found 270.0756.

Compound 23. *1-(3-Iodophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 1-(3-Iodophenyl)ethanone (1.00 g, 4.06 mmol) and dibromine (0.24 mL, 4.87 mmol) were mixed in chloroform (15 mL) to obtain the 2-bromo-1-(3-iodophenyl)-ethanone and this intermediate was reacted in a second time with morpholine (1.07 mL, 12.18 mmol) and sulfur (0.19 g, 6.09 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) to give the title compound as a yellow solid (0.75 g, 51%). R_f 0.3 (cyclohexane/EtOAc 8:2). Mp: 119-121°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.60-3.625 (t, 2H, $J = 4.8$ Hz), 3.70-3.72 (t, 2H, $J = 4.8$ Hz), 3.91-3.93 (t, 2H, $J = 4.8$ Hz), 4.31-4.33 (t, 2H, $J = 4.8$ Hz), 7.21-7.25 (DD, 1 ArH, $J = 7.8$ Hz), 7.92-7.94 (Dd, 2 ArH, $J = 7.1$ and 0.7 Hz), 8.32-8.33 (dd, 1 ArH, $J = 1.6$ Hz). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 46.60, 51.40, 65.79, 65.92, 93.94, 128.43, 129.94, 134.59, 137.76, 142.47, 185.29 (C=O), 193.88 (C=S).

Compound 24. *1-(2-Nitrophenyl)-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-(2-nitrophenyl)-ethanone (0.50 g, 2.05 mmol), morpholine (0.54 mL, 6.17 mmol), and sulfur (0.09 g, 3.07 mmol) in DMF (10 mL). A mixture of cyclohexane/EtOAc (8:2) was used for recrystallization to afford the title compound as a yellow solid
5 (0.15 g, 26%). R_f 0.3 (cyclohexane/EtOAc 8:2). Mp: 140-142°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.86-3.88 (t, 2H, $J = 4.8$ Hz), 3.94-3.96 (t, 2H, $J = 4.8$ Hz), 4.11-4.13 (t, 2H, $J = 4.8$ Hz), 4.22-4.24 (t, 2H, $J = 4.8$ Hz), 7.62-7.66 (m, 1 ArH), 7.74-7.78 (m, 1 ArH), 7.84-7.86 (m, 1 ArH), 8.04-8.06 (m, 1 ArH). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 49.06, 52.33, 66.36, 66.71, 123.84, 131.70, 132.57, 134.03, 134.92, 145.78, 182.95 (C=O), 191.17 (C=S). HRMS (ESI⁺): m/z calcd for
10 $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$ (M + H)⁺ 281.0590, found 281.0586.

Compound 25. *1-Cyclohexyl-2-morpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 1-cyclohexylethanone (2.00 g, 15.86 mmol) and dibromine (0.96 mL, 19.03 mmol) were mixed in chloroform (20 mL) to obtain the 2-bromo-1-cyclohexylethanone and this intermediate was reacted in a second time with morpholine (4.18 mL,
15 47.58 mmol) and sulfur (0.76 g, 23.79 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) to give the title compound as a brown solid (0.58 g, 15%). R_f 0.3 (cyclohexane/EtOAc 8:2). Mp: 57-59°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 1.18-1.37 (m, 5H), 1.69-1.99 (m, 5H), 3.22 (m, 1H), 3.61-3.63 (t, 2H, $J = 4.8$ Hz), 3.73-3.75 (t, 2H, $J = 4.8$ Hz), 3.83-3.85 (t, 2H, $J = 4.8$ Hz), 4.20-4.22 (t, 2H, $J = 4.8$ Hz). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm)
20 25.52 (2C), 25.71, 28.10 (2C), 47.28, 47.49, 52.07, 66.31, 66.60, 197.85 (C=O), 201.05 (C=S). HRMS (ESI⁺): m/z calcd for $\text{C}_{12}\text{H}_{19}\text{NO}_2\text{S}$ (M + H)⁺ 242.1209, found 242.1208.

Compound 26. *1-phenyl-2-thiomorpholino-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-phenyl-ethanone (1.00 g, 5.05 mmol), thiomorpholine (1.52 mL, 15.15 mmol), and sulfur (0.24 g, 7.57 mmol) in DMF (10 mL). The residue
25 was purified by silica gel chromatography (hexane/EtOAc, 9:1) to give the title compound as a brown solid (0.40 g, 43%). Mp: 128-130°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 2.69 (br s, 2H), 2.88-2.90 (t, 2H, $J = 4.8$ Hz), 3.83-3.86 (t, 2H, $J = 4.8$ Hz), 4.59 (br s, 2H), 7.47-7.51 (m, 2 ArH), 7.59-7.63 (m, 1 ArH), 7.97-7.99 (m, 2 ArH). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 27.31, 28.25, 49.71, 54.64, 128.96 (2C), 129.90 (2C), 133.23, 134.44, 187.73 (C=O), 196.06 (C=S). HRMS (ESI⁺): m/z calcd for
30 $\text{C}_{12}\text{H}_{13}\text{NOS}_2$ (M + H)⁺ 252.0511, found 252.0512.

Compound 27. *1-Phenyl-2-(4-phenylpiperazin-1-yl)-2-thioxoethanone*. This compound was synthesized according to the I described herein using 2-bromo-1-phenyl-ethanone (1.00 g, 5.05 mmol), 1-phenylpiperazine (2.31 mL, 15.15 mmol), and sulfur (0.24 g, 7.57 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (hexane/EtOAc, 9:1) to give the title
35 compound as a brown solid (0.20 g, 13%). R_f 0.4 (hexane/EtOAc 8:2). Mp: 87-89°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.20-3.22 (t, 2H, $J = 4.8$ Hz), 3.40-3.43 (t, 2H, $J = 4.8$ Hz), 3.73-3.76 (t, 2H, $J = 4.8$ Hz), 4.46-4.48 (t, 2H, $J = 4.8$ Hz), 6.92-6.96 (m, 3 ArH), 7.28-7.33 (m, 2 ArH), 7.47-7.52 (m, 2 ArH), 7.59-7.62 (m, 1 ArH), 8.00-8.20 (m, 2 ArH). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 45.06,

47.45, 48.10, 49.66, 115.28 (2C), 119.55, 126.78 (2C), 127.30 (2C), 127.74 (2C), 128.24 (2C), 131.65, 132.77, 148.47, 186.30 (C=O), 193.88 (C=S).

Compound 28. *2,2'-(Piperazine-1,4-diyl)bis(1-phenyl-2-thioxoethanone)*. This compound was synthesized according to the general procedure I using 2-bromo-1-phenyl-ethanone (1.00 g, 5.05 mmol), piperazine (1.30 g, 15.15 mmol), and sulfur (0.24 g, 7.57 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (hexane/EtOAc, 9:1) to give the title compound as a yellow solid (0.60 g, 31%). R_f 0.7 (cyclohexane/EtOAc 8:2). Mp > 250°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.65 (br s, 2H), 3.82-3.85 (t, 2H, J = 4.8 Hz), 4.38 (br s, 2H), 4.56 (br s, 2H), 7.42-7.53 (m, 4 ArH), 7.59-7.70 (m, 2 ArH), 7.91-8.20 (m, 4 ArH). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 43.44, 44.12, 47.61, 48.30, 126.63, 126.67, 127.46, 127.51, 130.45, 130.53, 132.35, 132.40, 185.41 (C=O), 185.48 (C=O), 194.72 (C=S), 194.80 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_2\text{S}_2$ ($\text{M} + \text{H}$) $^+$ 383.0882, found 383.0881.

Compound 29. *2-(4-(2-oxo-2-phenylethyl)piperazin-1-yl)-1-phenyl-2-thioxoethanone*. This compound was synthesized according to the general procedure I using 2-bromo-1-phenyl-ethanone (1.00 g, 5.05 mmol), piperazine (1.30 g, 15.15 mmol), and sulfur (0.24 g, 7.57 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography (hexane/EtOAc, 9:1) to give the title compound as orange oil (0.40 g, 22%). R_f 0.2 (cyclohexane/EtOAc 8:2). ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 2.67-2.70 (t, 2H, J = 4.8 Hz), 2.87-2.90 (t, 2H, J = 4.8 Hz), 3.66-3.69 (t, 2H, J = 4.8 Hz), 4.40-4.43 (t, 2H, J = 4.8 Hz), 7.42-7.53 (m, 4 ArH), 7.58-7.64 (m, 2 ArH), 7.94-8.15 (m, 4 ArH). HRMS (ESI $^+$): m/z calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$ ($\text{M} + \text{H}$) $^+$ 353.1318, found 353.1318.

Compound 30. *1-([1,1'-biphenyl]-4-yl)-2-(4-methylpiperazin-1-yl)-2-thioxoethanone*. This compound was synthesized according to the general procedure I. 4-Phenylacetophenone (2.00 g, 10.19 mmol) and dibromine (0.62 mL, 12.29 mmol) were mixed in chloroform (20 mL) to obtain the 2-bromo-1-cyclohexylethanone and this intermediate was reacted in a second time with N-methylpiperazine (3.38 mL, 30.06 mmol) and sulfur (0.48 g, 15.28 mmol) in DMF (10 mL). The residue was purified by silica gel chromatography ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 5:5) to give the title compound as a yellow solid (1.10 g, 32%). R_f 0.3 ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 5:5). Mp: 115-117°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 2.35 (s, 3H), 2.48 (br s, 2H), 2.68 (br s, 2H), 3.64 (br s, 2H), 4.35 (br s, 2H), 7.38-7.51 (m, 3 ArH), 7.59-7.65 (m, 2 ArH), 7.66-7.72 (m, 2 ArH), 8.05-8.08 (m, 2 ArH). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 44.74, 45.84, 50.53, 53.19, 53.84, 126.44 (2C), 126.67 (2C), 127.66, 128.15 (2C), 129.56 (2C), 131.14, 131.30, 138.68, 146.16, 186.71 (C=O), 194.48 (C=S). HRMS (ESI $^+$): m/z calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}\text{S}$ ($\text{M} + \text{H}$) $^+$ 325.1369, found 325.1370.

Compound 31. *4-(2-morpholino-2-thioxoacetyl)benzonitrile*. This compound was synthesized according to the general procedure I using 4-(2-bromoacetyl)benzonitrile (3.00 g, 13.45 mmol), morpholine (3.55 mL, 40.36 mmol), and sulfur (0.64 g, 20.17 mmol) in DMF (20 mL). Ethanol was used for recrystallization to afford the title compound as a yellow solid (1.60 g, 46%). R_f 0.1 (cyclohexane/EtOAc 8:2). Mp: 160-162°C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.62-3.63 (t, J = 4.7 Hz), 3.72-3.75 (t, J = 4.7 Hz), 3.92-3.94 (t, J = 4.7 Hz), 4.33-4.35 (t, J = 4.7 Hz), 7.78-7.80 (d, 2 ArH,

$J = 8.3$ Hz), 8.09-8.11 (d, 2 ArH, $J = 8.3$ Hz). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} (ppm) 45.05, 49.79, 64.10, 64.26, 115.03, 115.42, 127.88 (2C), 130.39 (2C), 134.53, 182.71 (C=O), 191.53 (C=S).

General procedure II. Bis(trichloromethyl) carbonate (1.00 g, 3.42 mmol) was added to a solution of benzotriazole (1.23 g, 10.30 mmol) and TEA (1.5 mL) in CH_2Cl_2 (15 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 1 h. Then, a solution of appropriate amine (8.2 mmol) and TEA (1.0 mL) in CH_2Cl_2 (15 mL) was added dropwise, and the reaction mixture was stirred at room temperature overnight. The reaction was quenched by adding a saturated NaHCO_3 solution and extracted with CH_2Cl_2 . The organic phase was dried over Na_2SO_4 , and evaporated *in vacuo* to give a residue which was chromatographed on silica gel (CH_2Cl_2 /hexane 98:2).

- 10 **Compound 32.** *N*-(4-fluorophenethyl)-1*H*-benzo[d][1,2,3]triazole-1-carboxamide. Following general procedure II, white solid (2.13 g, 73 %) was obtained. Mp: 129-131 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 2.96 (m, 2H), 3.60-3.62 (m, 2H), 7.10-7.34 (m, 4 ArH), 7.53-7.57 (m, 1 ArH), 7.70-7.73 (m, 1 ArH), 8.17-8.21 (m, 2 ArH), 9.32 (br s, NH).

- 15 **Compound 33.** *Piperazine-1,4-diylbis((1H-benzo[d][1,2,3]triazol-1-yl)methanone)*. Following general procedure II, white solid (1.40 g, 48%) was obtained. Mp: 138-140 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 4.02 (br s, 8H), 7.55-7.59 (dd, 1 ArH, $J = 7.3$ Hz), 7.72-7.76 (dd, 1 ArH, $J = 7.3$ Hz), 7.99-8.01 (d, 1 ArH, $J = 8.3$ Hz), 8.22-8.24 (dd, 1 ArH, $J = 8.3$ Hz).

- 20 General procedure III. To a solution of *N,N*-dimethylglycine (30 mol %), dithiocarbamic acid sodium salt (1.2 eq), obtained as reported by Sattigeri *et al.* (ARKIVOC, 2005, No. ii, 46-59), and substituted aryl iodide (1 eq) in anhydrous DMF was added CuI (15 mol %). Under nitrogen atmosphere, the mixture was stirred at 110 °C for 24h. The reaction was then cooled at room temperature, poured in water and extracted with EtOAc. The combined organic layer was dried over MgSO_4 . After evaporation of solvent, the product was purified by silica gel chromatography (petroleum ether/ethyl ether 4:1) to give the target compound.

- 25 **Compound 34.** *Phenyl 4-cinnamylpiperazine-1-carbodithioate*. Following general procedure III, white solid (0.95 g, 55%) was obtained. Mp: 101-103 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 2.54 (br s, 4H), 3.18 (d, 2H, $J = 6.8$ Hz), 3.98-4.20 (br s, 2H), 4.20-4.45 (br s, 2H), 6.20-6.25 (m, 1H), 6.48-6.52 (d, 1H, $J = 15.8$ Hz), 7.20-7.48 (m, 10 ArH).

- 30 **Compound 35.** *Phenyl 4-phenylpiperazine-1-carbodithioate*. Following general procedure III, white solid (1.37 g, 89%) was obtained. Mp: 159-161 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.15-3.19 (br s, 4H), 4.05-4.20 (br s, 2H), 4.20-4.52 (br s, 2H), 6.82-6.91 (m, 3 ArH), 7.22-7.28 (m, 2 ArH), 7.38-7.44 (m, 5 ArH).

- 35 **Compound 36.** *2,4-dinitrophenyl 4-(4-methoxyphenyl)piperazine-1-carbodithioate*. Following general procedure III, yellow solid (0.46 g, 63%) was obtained. Mp: 123-125 °C. ^1H NMR (400 MHz, CDCl_3): δ_{H} (ppm) 3.21-3.24 (br s, 4H), 3.70 (s, 3H), 4.20 (br s, 2H), 4.36 (br s, 2H), 6.85-6.96 (m, 4 ArH), 8.01-8.03 (d, 1 ArH, $J = 8.6$ Hz), 8.54-8.56 (dd, 1 ArH, $J = 2.1$ and 8.6 Hz), 8.88 (d, 1 ArH, $J = 2.1$ Hz).

Compound 37. *4-nitrophenyl dibenzylcarbamodithioate*. Following general procedure III, yellow solid (0.57 g, 72%) was obtained. Mp: 130-132°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 4.99 (s, 2H), 5.25 (s, 2H), 7.21-7.40 (m, 10 ArH), 7.65 (d, 2 ArH, *J* = 8.1 Hz), 8.23 (d, 2 ArH, *J* = 8.1 Hz).

Compound 38. *3-bromophenyl dibenzylcarbamodithioate*. Following general procedure III, white solid (0.61 g, 81%) was obtained. Mp: 73-75°C. ¹H NMR (400 MHz, CDCl₃): δ_H (ppm) 4.99 (s, 2H), 5.25 (s, 2H), 7.20-7.38 (m, 11 ArH), 7.41 (ddd, 1 ArH, *J* = 1.3 and 7.8 Hz), 7.55 (m, 1 ArH), 7.62 (dd, 1 ArH, *J* = 1.8 Hz).

Example 2. Development of a fluorescent biochemical assay.

PHGDH oxidizes 3-PG to 3-PPyr with NAD⁺ as the electron acceptor to yield NADH. The formation of 3-PG is directly correlated with the NADH formation (Ex 340 nm / Em 460 nm). Thus, the enzymatic activity of PHGDH can be monitored by following the fluorescence intensity at an excitation wavelength of 360 nm and emission wavelength of 460 nm.

PHGDH activity was screened at varying enzyme concentration, cofactor concentration and substrate concentration by monitoring the oxidation of NADH spectrophotometrically. The tolerance of the enzymatic assay to DMSO was studied at a DMSO concentration ranging from 5% to 20% (Fig. 1). For this present study, the concentrations of Tris HCl pH 8.8, NaCl and DTT were fixed at 100 mM, 400 mM and 0.2 mM respectively and the temperature was kept at 25°C.

Minimizing enzyme usage was an important consideration for controlling the cost of assays. So, we sought to determine enzyme concentrations that would generate a sufficient fluorescent signal. Representative progress curves obtained with PHGDH quantity ranging from 1 ng to 100 ng, are shown in Fig 1A. As depicted, a quantity of 100 ng of PHGDH was sufficient to achieve a robust assay window. The concentration of 3-PG and NAD⁺ in an assay is also an important consideration. Concentration of 3-PG was varied between 0.25 and 2.5 mM and two concentrations of NAD⁺ were evaluated (Fig 1B and Fig 1C). Optimal concentrations of 3-PG and NAD were 0.5 mM and 1 mM respectively to detect a correct fluorescent signal. Compounds from the database were stored at 10 mM in DMSO and diluted in DMSO prior to the experiments to a final concentration of 10 μM in the reaction wells. Thus, the final concentration of DMSO in assay solutions was 10%. As depicted in Fig. 1D, this percentage of DMSO was tolerated by PHGDH. Finally, the final optimized conditions consisted of PHGDH (100 ng), 3-PG (0.5 mM), and NAD (1 mM). In these conditions, the rate of substrate conversion was found to be linear during the five first minutes.

The K_m value of 3-PG was then determined by fitting the data to the Michaelis–Menten equation. The calculated K_m value (0.19 ± 0.03 mM) was similar of the reported K_m values of 0.26 ± 0.03 mM.

Example 3. *In vitro* PHGDH inhibition assay.

The purities of the final compounds involved in biological assays were at least 95%.

PHGDH inhibition assay was performed in black polypropylene 96-well plates (Sigma-Aldrich) using NAD (Sigma-Aldrich) as cofactor and 3-phosphoglycerate (Sigma-Aldrich) as substrate. Tested compounds were dissolved in DMSO. The final concentration of DMSO in assay solutions was 10 %,

which was shown to have no effect on PHGDH activity. The reaction volume per well was 50 μ L. Each assay was carried out in triplicate. Briefly, a solution buffer (100 mM Tris HCl buffer (pH 8.8), 400 mM NaCl, 0.2 mM DTT, 1 mM NAD and 0.5 mM 3-PG) was added at various concentrations of tested compounds. Then, an amount of 100 ng of PHGDH (human recombinant protein, BPS Bioscience) was added to start the reaction. Finally, the product formation, correlated with NADH formation, was instantly monitored for 7 min at 25°C using a SpectraMax spectrophotometer at an excitation wavelength of 360 nm and emission wavelength of 460 nm. Compounds were initially screened at a single concentration of 100 μ M or 10 μ M in duplicate. Compounds showing promising inhibition potency at those concentrations, an IC₅₀ was determined. The obtained results are in table 2 below.

Table 2

Compound number	% inh. (100 μ M)	% inh. (10 μ M)	IC ₅₀ (μ M)
4	93%		1.9
5		20	
6		85	1.2
7		23	
8		25	
11		68	
12		73	
13		36	
33	46		
35		20	
36		23	
37		22	
38		21	
39	96		5.3
40	100		0.3
41	100		0.6
42	92		5.1
43	37		
44	51		
45	43		
46	33		
47	80		44.1
48	47		
49	59		
50	54		
51	26		
52		25	
53		30	
54		30	
55		25	
56		63	
57		39	
58		21	
59		21	
60		20	
61		25	
62		24	
63		39	

64		68	3.7
65		22	
66		50	8.1
67		64	
68		68	4.5
69		35	
70		60	
71		72	9.3
104	96		
105	50		

Example 4. Cellular evaluation of identified PHGDH inhibitors

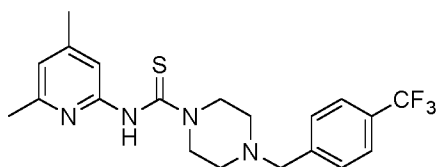
BT20 and MDA-MB-231 breast cancer cells

Cell models and cytotoxicity assay. All cell lines were acquired in the last 3 years from ATCC where they are regularly authenticated by short tandem profiling. Cells were stored according to the supplier's instructions and used within 6 months after resuscitation of frozen aliquots. BT-20 and MDA-MB-231 breast cancer cells were routinely cultured in DMEM containing serum and antibiotics. For the cytotoxicity assay, cells were treated, for 7 days at 37°C, with the synthesized compounds at a concentration range of 25-100 µM in MEM medium supplemented or not with 0.1 mM L-serine (Sigma-Aldrich). After 72h incubation, the medium was removed and replaced by freshly prepared compound-containing medium. Antiproliferative effects were determined using Presto Blue assay (Life Technologies) according to manufacturer's instructions.

The results are shown in Figures 2 and 3.

Example 5. Cell Models and Cytotoxicity Assay

All cell lines were acquired in the last three years from ATCC, where they are regularly authenticated by short tandem profiling. Cells were stored according to the supplier's instructions and used within 6 months after resuscitation of frozen aliquots. SiHa cervix carcinoma cells and MDA-MB-231 breast cancer cells were routinely cultured in DMEM supplemented with 10% FBS and antibiotics. For the cytotoxicity assay, cells were seeded at low density in 96-well plates in serine containing media. Media were then aspirated, and cells were incubated in fresh serine-replete or -deplete media containing drugs or vehicle (DMSO). Cells were grown for 5 days at 37°C with drug and media changed daily before assaying cell viability using a Presto Blue assay (Life Technologies) according to manufacturer's instructions. Figure 4 shows the ability of the selected cancer cell lines to proliferate in serine-replete or -deplete medium (Figure4: (A,C) Representative immunoblot for PHGDH. (B,D) Cell growth extent (for 5 days) in either serine-replete (+Ser) or serine-deplete (-Ser) medium. Data are shown as mean ± SEM (n≥3)).



Compound:

was used as control.

The obtained results are in tables 3 and 4.

Table 3: Cell Proliferation Inhibition on SiHa ($\pm$ Ser) and MDA-MB-231 (+Ser)

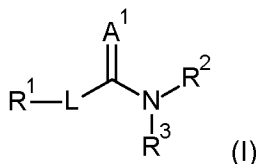
Compound	IC ₅₀ (95 % CI) (μ M)		
	SiHa		MDA-MB-231
	+ Ser	-Ser	+ Ser
Control	22.7 (19.4-26.9)	6.5 (5.5-7.6)	> 100
Control	71.7 (55.9-101.9)	7.9 (5.8-10.8)	> 100
40	> 100	> 100	> 100
17	> 100	43.3 (35.7-53.5)	> 100
65	> 100	> 100	> 100
18	21.0 (19.1-23.0)	6.6 (5.7-7.5)	> 100
66	20.4 (18.6-22.5)	7.9 (7.2-8.8)	> 100
68	26.1 (22.5-30.1)	12.6 (10.7-14.9)	36.1 (30.4-43.0)
39	22.7 (20.7-24.9)	7.5 (6.5-8.6)	> 100
47	> 100	57.5 (41.9-85.0)	> 100
49	38.2 (32.9-44.0)	28.1 (23.0-34.1)	52.4 (42.8-64.3)
41	25.7 (23.4-28.2)	9.3 (8.0-10.8)	> 100
11	22.8 (20.8-25.1)	7.6 (6.6-8.8)	> 100

Table 4 Cell Proliferation Inhibition on HL-60 shScr ($\pm$ Ser) and HL-60 shPHGDH (+Ser)

Compound	IC ₅₀ (95 % CI) (μ M)		
	HL-60 shScr		HL-60 shPHGDH
	+ Ser	-Ser	+ Ser
Control	47.5 (38.7-59.6)	10.1 (8.1-12.7)	> 100
40	> 100	18.3 (14.6-23.3)	> 100
17	> 100	> 100	> 100
65	> 100	64.4 (49.9-87.9)	> 100
18	> 100	> 100	> 100
66	50.5 (40.4-64.8)	15.5 (12.1-20.1)	> 100
68	37.2 (27.4-52.3)	16.9 (12.2-24.1)	> 100
39	24.3 (22.4-26.4)	7.0 (6.2-8.0)	> 100
47	25.2 (23.5-26.9)	8.3 (7.5-9.2)	> 100
49	> 100	83.0 (60.4-125.4)	> 100
41	41.6 (36.7-47.4)	33.1 (27.2-40.3)	58.8 (47.8-72.1)
11	19.6 (17.6-21.9)	7.1 (6.2-8.3)	> 100
67	17.6 (15.8-19.7)	6.0 (5.2-6.9)	> 100

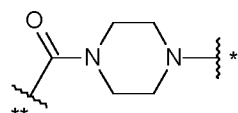
Claims

1. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof,



5 wherein,

A^1 is selected from the group consisting of S; and O;

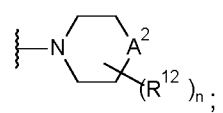
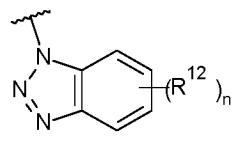
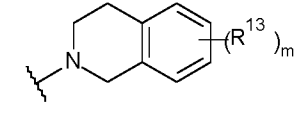
L is selected from the group consisting of $\text{C}=\text{O}$; S; NR^5 ; $^*\text{NR}^6-\text{NR}^7-\text{C}(\text{O})^{**}$; ; $\text{C}=\text{S}$; and a single bond; wherein * represents where L is bound to $\text{C}=\text{A}^1$; and ** represents where L is bound to R^1 ; and wherein,

10 R^1 is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^1 ;

R^2 is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^2 ;

R^3 is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z^3 ;

or R^2 and R^3 form together with the nitrogen to which they are attached a moiety selected from

20 the group consisting of ; ; ; wherein,

A^2 is selected from the group consisting of O; NR^9 ; NH; $\text{CR}^{10}\text{R}^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

25 R^9 is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl; heterocyclcarbonylalkyl; heterocyclcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

R^{10} is selected from the group consisting of halo, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or $S(O)_2$;

R^5 is selected from the group consisting of hydrogen, alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heteroaryheterocyclyl, heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^7 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at

least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl or aryl,
5 then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl or arylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH or S;

10 and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁹, O or S; R¹ is aryl; then L is not S;

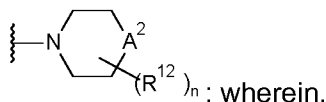
and with the proviso that said compound is not

- 15 - (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(4-phenylphenyl)-2-thioxo-ethanone;
- 4-benzyl-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carbothioamide;
- (3-chlorophenyl)-morpholino-methanethione;
- 20 - (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- morpholino N-phenylcarbamodithioate;
- 1-(4-fluorophenyl)-2-morpholino-2-thioxo-ethanone;
- 25 - 1-(4-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-nitrophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-bromophenyl)-2-morpholino-2-thioxo-ethanone;
- 1-(4-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 1-morpholino-2-phenyl-ethanethione;
- 30 - N-phenylmorpholine-4-carboxamide;
- (4-phenylphenyl)-(4-phenylpiperazin-1-yl)methanethione;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 35 - 2-(4-methyl-1-piperidyl)-1-phenyl-2-thioxo-ethanone;
- 4-(2-morpholino-2-thioxo-acetyl)benzoic acid;
- 1-morpholino-2-phenyl-ethane-1,2-dione;

- 2-hydroxy-1-morpholino-2-phenyl-ethanone;
- N-morpholinobenzamide;
- 1-morpholino-3-phenyl-urea;
- 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 5 - 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-morpholino-1-(p-tolyl)-2-thioxo-ethanone;
- 2-(4-ethylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-cyclohexyl-2-oxo-2-phenyl-thioacetamide;
- 1-(3-methoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 10 - 1-(4-ethoxyphenyl)-2-morpholino-2-thioxo-ethanone;
- 2-morpholino-1-(2-naphthyl)-2-thioxo-ethanone;
- 2-morpholino-1-(1-naphthyl)-2-thioxo-ethanone;
- 1-(2-furyl)-2-morpholino-2-thioxo-ethanone;
- 2-morpholino-1-(2-thienyl)-2-thioxo-ethanone;
- 15 - 1-(benzofuran-2-yl)-2-morpholino-2-thioxo-ethanone;
- 2-oxo-2-phenyl-N-(p-tolyl)thioacetamide;
- 2-oxo-N,2-diphenyl-thioacetamide;
- N-(4-fluorophenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-chlorophenyl)-2-oxo-2-phenyl-thioacetamide;
- 20 - N-(4-bromophenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-isopropylphenyl)-2-oxo-2-phenyl-thioacetamide;
- N-(4-methoxyphenyl)-2-oxo-2-phenyl-thioacetamide;
- 2-oxo-N-phenyl-2-(p-tolyl)thioacetamide;
- N-[3-[2-(1-piperidyl)-2-thioxo-acetyl]phenyl]acetamide;
- 25 - 1-(5-chloro-2-phenoxy-phenyl)-2-morpholino-2-thioxo-ethanone;
- 1-[2-(4-chlorophenoxy)phenyl]-2-morpholino-2-thioxo-ethanone;
- methyl 4-(2-morpholino-2-thioxo-acetyl)benzoate;
- 1-(2-chlorophenyl)-2-morpholino-2-thioxo-ethanone;
- 2-(2-chlorophenyl)-N,N-dimethyl-2-oxo-thioacetamide;
- 30 - 2-(4-chlorophenyl)-N,N-dimethyl-2-oxo-thioacetamide;
- N,N-dimethyl-2-(1-naphthyl)-2-oxo-thioacetamide;
- N-benzyl-N-methyl-2-oxo-2-phenyl-thioacetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;
- 35 - N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

2. The compound according to claim 1, wherein A¹ is S

3. The compound according to claim 1, wherein A¹ is O.
4. The compound according to any one of claims 1 to 3, wherein L is C=O.
5. The compound according to any one of claims 1 to 3, wherein L is S.
6. The compound according to any one of claims 1 to 3, wherein L is a single bond.
- 5 7. The compound according to any one of claims 1 to 6, wherein R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; haloalkyl; arylalkyl; heterocyclalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹.
8. The compound according to any one of claims 1 to 7, wherein R² and R³ form together with the nitrogen to which they are attached a moiety selected from the group consisting of



A² is selected from the group consisting of O; NR⁹; NH; CR¹⁰R¹¹; and S;

n is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; alkyl; cycloalkyl; arylalkyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclalkyl; heterocyclcarbonylalkyl; heterocyclcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴; each Z⁴ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁴ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

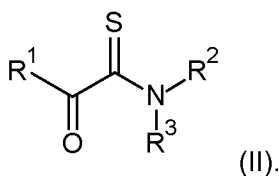
R¹⁰ is selected from the group consisting of halo, alkyl, alkenyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be unsubstituted or substituted with one or more Z⁵; each Z⁵ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁵ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and

wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

R¹¹ is selected from the group consisting of halo, hydrogen, alkyl, haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹; cyano; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NO₂; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; wherein each group can be unsubstituted or substituted with one or more Z⁶; each Z⁶ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z⁶ together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

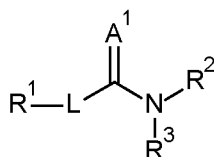
each R¹² is independently selected from the group consisting of hydrogen; halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two R¹² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂.

9. The compound according to any one of claims 1, 2, 4, 7, 8, having formula (II)



10. A pharmaceutical composition comprising one or more pharmaceutically acceptable excipients and a therapeutically effective amount of a compound according to any one of claims 1 to 9.

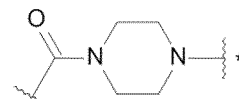
11. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use as a medicament,



(I)

wherein,

A¹ is selected from the group consisting of S; O; and NR⁴;



L is selected from the group consisting of C=O; S; O; NR⁵; *NR⁶-NR⁷-C(O)**; ** ;

5 C=S; and a single bond; wherein * represents where L is bound to C=A¹; and ** represents where L is bound to R¹; and wherein,

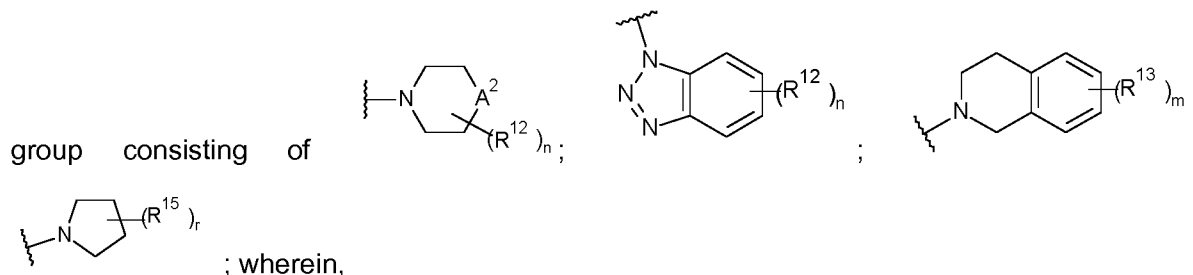
R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclylalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

10 R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein

15 each group can be unsubstituted or substituted with one or more Z³;

or R² and R³ form together with the nitrogen to which they are attached a moiety selected from the



A² is selected from the group consisting of O; NR⁹; CR¹⁰R¹¹; and S;

20 n is an integer selected from 0, 1, 2, or 3;

m is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R⁹ is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z⁴;

R¹⁰ is selected from the group consisting of halo; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; -NR¹⁶R¹⁷; -OR¹⁸; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; -SR¹⁹;

30

cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{OR}^{18}$; heterocyclyl; heterocyclalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-\text{SR}^{19}$; cyano; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NO}_2$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

each R^{12} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-\text{NO}_2$; aryl; cycloalkyl; cyano; hydroxyl; $-\text{OR}^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-\text{NR}^{16}\text{R}^{17}$; $-\text{SR}^{19}$; carboxyl; $-\text{CO}_2\text{R}^{20}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{17}$; $-\text{C}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})\text{R}^{20}$; $-\text{S}(\text{O})_2\text{R}^{20}$; $-\text{SO}_2\text{NR}^{16}\text{R}^{17}$; $-\text{NHC}(\text{O})\text{R}^{20}$; $-\text{NHS}(\text{O})_2\text{R}^{20}$; and $-\text{NHC}(\text{O})\text{NR}^{16}\text{R}^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{N}=\text{O}$, $\text{N}=\text{S}$, $\text{S}=\text{O}$ or $\text{S}(\text{O})_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-\text{OR}^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁶ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R⁷ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

5 each R¹⁶ is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; 10 alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 15 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, 20 heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl 25 moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or 30 S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; heteroaryheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; 35 carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl;

heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^2 together with the atom to which they are attached can
 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom
 5 or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at
 least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 10 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can
 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom
 or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at
 least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

15 each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS$
 $(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can
 20 form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom
 or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be oxidized to form at
 least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 25 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-N$
 $HS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached
 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one
 carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be
 30 oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano;
 hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclalkyl;
 heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;
 35 carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-N$
 $HS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached
 can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one
 carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclalkyl; heteroaryl moiety can be
 oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^7 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$;

carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-N$

- 5 $HS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

- 10 and with the proviso that for a compound of formula (I) when A^1 is O; R^1 is heteroaryl, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A^1 is S; R^1 is heteroarylalkyl or arylalkyl; A^2 is O, then L is not a single bond;

- and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is
15 unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; R^2 is cycloalkyl; R^1 is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is O; R^1 is unsubstituted aryl, then L is not NH;

- 20 and with the proviso that for a compound of formula (I) when A^1 is S; A^2 is NR^9 or S; R^1 is aryl; then L is not S;

and with the proviso that said compound is not

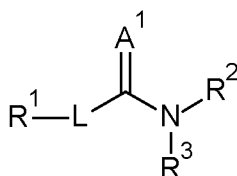
- (3,4-dichlorophenyl)-morpholino-methanethione;
- 2-morpholino-1-phenyl-2-thioxo-ethanone;
- 25 - (3-chlorophenyl)-morpholino-methanethione;
- (2,4-dinitrophenyl) morpholine-4-carbodithioate;
- (2,4-dinitrophenyl) N-benzyl-N-methyl-carbamodithioate;
- 4-benzhydryl-N-(4-nitrophenyl)piperazine-1-carbothioamide;
- (2,4-dinitrophenyl) N,N-dicyclohexylcarbamodithioate;
- 30 - morpholino N-phenylcarbamodithioate;
- 1-cyclohexyl-3-(4-phenylthiazol-2-yl)urea;
- 2-cyclohexyl-N-(4-phenylthiazol-2-yl)acetamide;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 35 - 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-[3-[2-(1-piperidyl)-2-thioxo-acetyl]phenyl]acetamide
- N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;

- N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

12. A compound for use according to claim 11, wherein said compound is a compound according to

5 any one of claims 1 to 9.

13. A compound of formula (I), a stereoisomer thereof, an enantiomer thereof, a racemic thereof, or a tautomer thereof, for use in the prevention or treatment of a cellular proliferative disease,

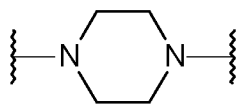
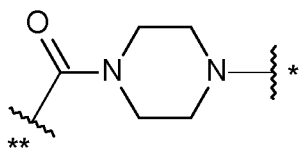


(I)

10 wherein,

A¹ is selected from the group consisting of S; O; and NR⁴;

L is selected from the group consisting of C=O; S; O; NR⁵; *NR⁶-NR⁷-C(O)**; NR⁶-NR⁷;



; C=S; a single bond; C=NR⁸; and SO₂; wherein *

represents where L is bound to C=A¹; and ** represents where L is bound to R¹; and wherein,

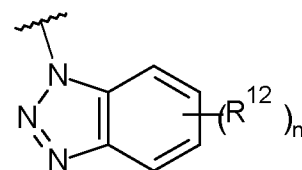
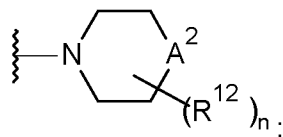
15 R¹ is selected from the group consisting of aryl; cycloalkyl; heteroaryl; heterocyclyl; alkyl; alkenyl; alkynyl; haloalkyl; haloalkyloxy; arylalkyl; heterocyclylalkyl; heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z¹;

R² is selected from the group consisting of arylalkyl; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein

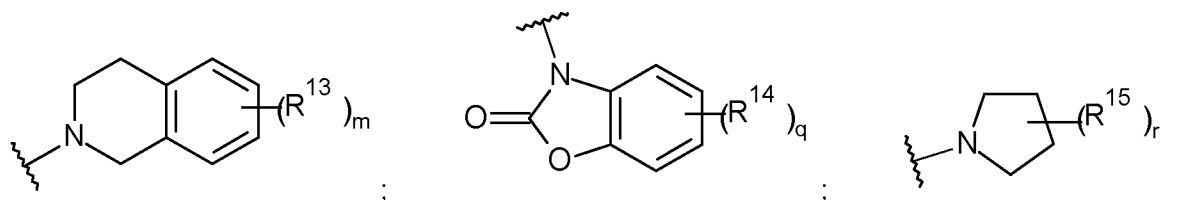
20 each group can be unsubstituted or substituted with one or more Z²;

R³ is selected from the group consisting of arylalkyl; hydrogen; alkyl; alkenyl; alkynyl; cycloalkyl; aryl; arylalkenyl; arylalkynyl; heterocyclyl; heterocyclylalkyl; heteroaryl; and heteroarylalkyl; wherein each group can be unsubstituted or substituted with one or more Z³;

or R² and R³ form together with the nitrogen to which they are attached a moiety selected from the



25 group consisting of



wherein,

A^2 is selected from the group consisting of O; NR^9 ; $CR^{10}R^{11}$; and S;

n is an integer selected from 0, 1, 2, or 3;

5 m is an integer selected from 0, 1, 2, or 3;

q is an integer selected from 0, 1, 2, or 3;

r is an integer selected from 0, 1, 2, or 3;

R^9 is selected from the group consisting of aryl; hydrogen; alkyl; cycloalkyl; arylalkyl; arylalkenyl; arylalkynyl; arylcarbonylalkyl; arylcarbonylthiocarbonyl; heterocyclyl; heterocyclylalkyl; heterocyclylcarbonylalkyl; heterocyclylcarbonylthiocarbonyl; heteroaryl; heteroarylalkyl; heteroarylcarbonylalkyl; heteroarylcarbonylthiocarbonyl; wherein each group can be unsubstituted or substituted with one or more Z^4 ;

10 R^{10} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^5 ;

15 R^{11} is selected from the group consisting of halo, hydrogen, alkyl, alkenyl; alkynyl; haloalkyl; haloalkyloxy; cycloalkyl; aryl; arylalkyl; hydroxyl; $-NR^{16}R^{17}$; $-OR^{18}$; heterocyclyl; heterocyclylalkyl; heteroaryl; heteroarylalkyl; carboxyl; $-SR^{19}$; cyano; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NO_2$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; wherein each group can be unsubstituted or substituted with one or more Z^6 ;

20 each R^{12} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{12} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R^{13} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{13} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{14} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{14} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each R^{15} is independently selected from the group consisting of hydrogen; halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two R^{15} together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

R^4 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

R^5 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^6 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^7 is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl;

R^8 is selected from the group consisting of alkyl; hydroxyl; $-OR^{18}$; cycloalkyl; arylalkyl; heterocyclalkyl; and heteroarylalkyl;

each R^{16} is independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclalkyl; and heteroarylalkyl; wherein at

least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁷ is independently selected from the group consisting of hydrogen; -NH₂; alkyl; alkylaminoalkyl; hydroxyalkyl, alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or R¹⁶ and R¹⁷ form together with the nitrogen to which they are attached, a saturated or unsaturated 4-, 5-, or 6-membered ring, said saturated or unsaturated ring can be unsubstituted or substituted with one or more Z⁷;

each R¹⁸ is independently selected from the group consisting of alkyl; aryl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; heteroarylalkyl; and cyanoalkyl; wherein at least one carbon atom or heteroatom of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R¹⁹ is independently selected from the group consisting of aryl; alkyl; alkenyl; alkynyl, cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; or heteroaryl moiety; can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each R²⁰ is independently selected from the group consisting of hydrogen; hydroxyl; alkyl; alkenyl; alkynyl; aryl; cycloalkyl; arylalkyl; heterocyclyl; heteroaryl; heterocyclylalkyl; and heteroarylalkyl; wherein at least one carbon atom or heteroatom of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z¹ is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; heteroaryheterocyclyl, -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷;

each Z² is independently selected from the group consisting of halo; -NO₂; aryl; cycloalkyl; cyano; hydroxyl; -OR¹⁸; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; -NR¹⁶R¹⁷; -SR¹⁹; carboxyl; -CO₂R²⁰; -C(O)NR¹⁶R¹⁷; -C(O)R²⁰; -S(O)R²⁰; -S(O)₂R²⁰; -SO₂NR¹⁶R¹⁷; -NHC(O)R²⁰; -NHS(O)₂R²⁰; and -NHC(O)NR¹⁶R¹⁷; or two Z² together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

each Z^3 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^3 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^4 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^4 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^5 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^5 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^6 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^6 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one $C=O$, $C=S$, $N=O$, $N=S$, $S=O$ or $S(O)_2$;

each Z^7 is independently selected from the group consisting of halo; $-NO_2$; aryl; cycloalkyl; cyano; hydroxyl; $-OR^{18}$; alkyl; haloalkyl; haloalkyloxy; arylalkyl; heteroaryl; heteroarylalkyl; heterocyclyl; heterocyclylalkyl; $-NR^{16}R^{17}$; $-SR^{19}$; carboxyl; $-CO_2R^{20}$; $-C(O)NR^{16}R^{17}$; $-C(O)R^{20}$; $-S(O)R^{20}$; $-S(O)_2R^{20}$; $-SO_2NR^{16}R^{17}$; $-NHC(O)R^{20}$; $-NHS(O)_2R^{20}$; and $-NHC(O)NR^{16}R^{17}$; or two Z^7 together with the atom to which they are attached can form a saturated or unsaturated 5-, 6-, or 7-membered ring; and wherein at least one

carbon atom or heteroatom of alkyl; cycloalkyl, aryl, heterocyclyl; heteroaryl moiety can be oxidized to form at least one C=O, C=S, N=O, N=S, S=O or S(O)₂;

or a solvate thereof, a hydrate thereof, or a pharmaceutically acceptable salt thereof;

and with the proviso that for a compound of formula (I) when A¹ is O; R¹ is heteroaryl, then L is not a
5 single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R¹ is heteroarylalkyl; A² is O, then L is not a single bond;

and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

10 and with the proviso that for a compound of formula (I) when A¹ is S; R² is cycloalkyl; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is O; R¹ is unsubstituted aryl, then L is not NH;

and with the proviso that for a compound of formula (I) when A¹ is S; A² is NR⁰; R¹ is aryl; then L is
15 not S;

and with the proviso that said compound is not

- 2-(4-benzhydrylpiperazin-1-yl)-1-(4-nitrophenyl)-2-thioxo-ethanone;
- 2-(4-benzhydrylpiperazin-1-yl)-1-phenyl-2-thioxo-ethanone;
- N-(4-methyl-2-pyridyl)-4-[4-(trichloromethyl)phenyl]piperazine-1-carbothioamide;
- 20 - N-(4,6-dimethyl-2-pyridyl)-4-[5-(trichloromethyl)-2-pyridyl]piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-(4-pyridyl)piperazine-1-carbothioamide;
- N-(4,6-dimethyl-2-pyridyl)-4-[[4-(trichloromethyl)phenyl]methyl]piperazine-1-carbothioamide.

14. A compound for use according to claim 13, wherein said compound is a compound according to any one of claims 1 to 9.

25 15. The compound for use according to any one of claims 13 to 14, wherein said cellular proliferative disease is cancer.

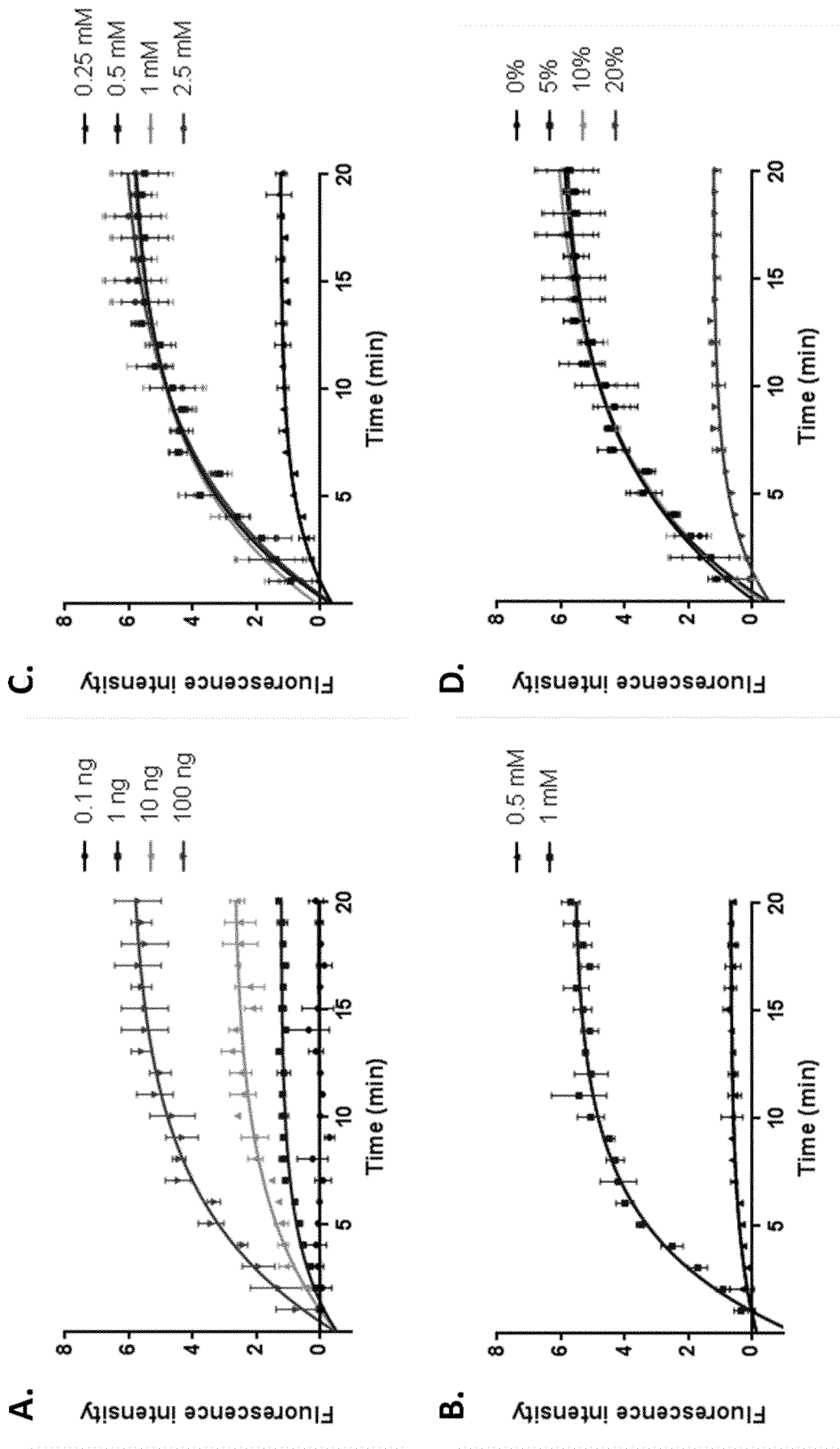


FIG. 1

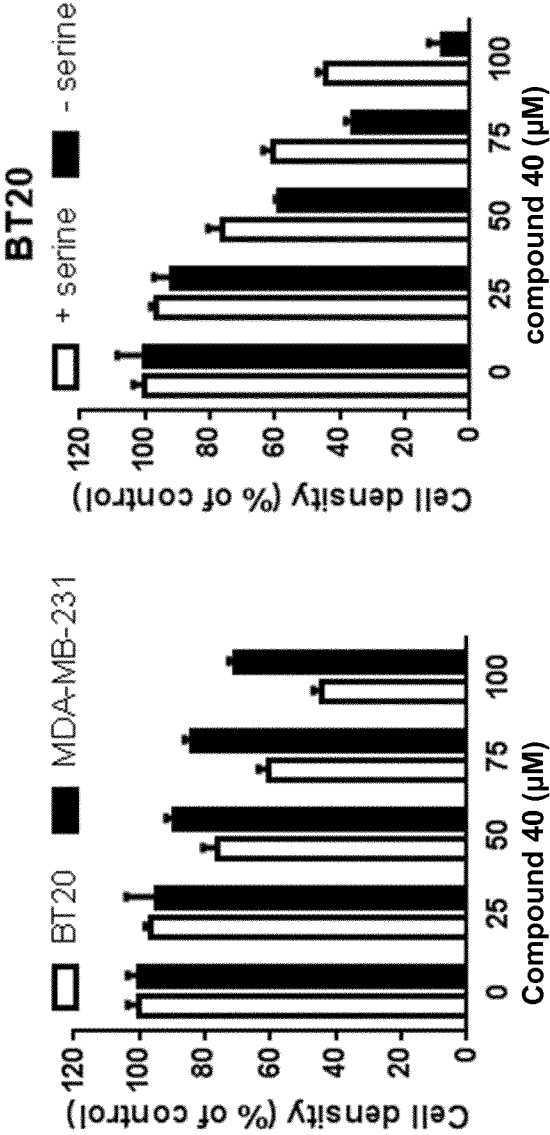


FIG. 3

FIG. 2

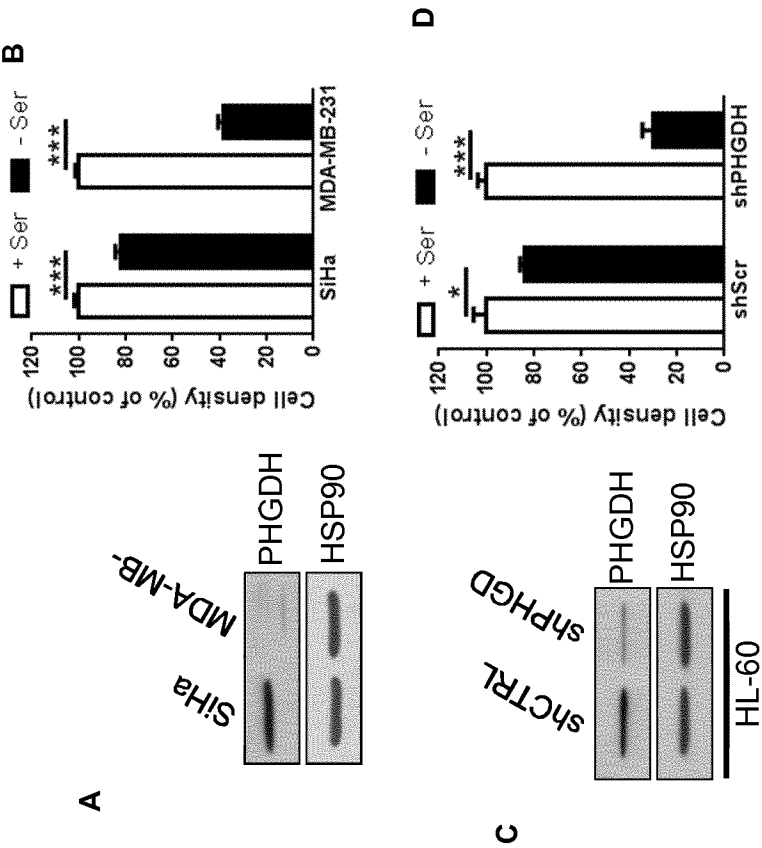


FIG. 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/055898

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D413/12 C07D295/14 A61K31/495 A61K31/5375 A61K31/54
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	C.N. KAPANDA ET AL.: "Synthesis and pharmacological evaluation of 2,4-dinitroaryldithiocarbamate derivatives as novel monoacylglycerol lipase inhibitors", JOURNAL OF MEDICINAL CHEMISTRY, vol. 55, 31 May 2012 (2012-05-31), pages 5774-5783, XP002759525, compounds 03-04 with A1 = S, L = C(0); R1 = Ph, NO2-Ph; A2 = N-C(Ph)2; n = 0; the whole document ----- -/--	1,2,4, 7-15



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

4 May 2017

Date of mailing of the international search report

13/07/2017

Name and mailing address of the ISA/

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Authorized officer

Seelmann, Marielle

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2017/055898

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LI HONG-ZHENG ET AL: "Direct synthesis of [alpha]-ketothioamides from aryl methyl ketones and amines via I2-promoted sp ³ C-H functiona", TETRAHEDRON, vol. 70, no. 31, 20 May 2014 (2014-05-20), pages 4645-4651, XP028848193, ISSN: 0040-4020, DOI: 10.1016/J.TET.2014.05.045 scheme 3; the whole document	1,2,4, 7-10
X	V. S. VELEZHEVA ET AL.: J. HETEROCYCLIC. CHEM., vol. 50, 1 January 2013 (2013-01-01), pages 225-236, XP002759526, compound 6, scheme 1	1,2,4, 7-9
X	HARRIS T W ET AL: "AFFINITY OF 10-(4-METHYLPIPERAZINO)DIBENZ not B,F 3/4 OXEPINS FOR CLOZAPINEAND SPIROPERIDOL BINDING SITES IN RAT BRAIN", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 25, no. 7, 1 January 1982 (1982-01-01), pages 855-858, XP001012760, ISSN: 0022-2623, DOI: 10.1021/JM00349A018 compounds 10a-b	1,2,4, 7-9
X	CN 102 653 619 A (UNIV NANJING FORESTRY) 5 September 2012 (2012-09-05) compounds 1-14	1,2,4, 7-9
X	U. C. KASSÉHIN ET AL.: "Insight into the Willgerodt-Kindler reaction of gamma-haloacetophenone derivatives", ORG. CHEM. INT., 486540, 10 December 2014 (2014-12-10), pages 1-5, XP002759527, the whole document	1,2,4, 7-15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/055898

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

4, 9(completely); 1, 2, 7, 8, 10-15(partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 4, 9(completely); 1, 2, 7, 8, 10-15(partially)
oxothioamides covering A1 = S, L = C(O)

2. claims: 5(completely); 1, 2, 7, 8, 10-15(partially)
dithiocarbamates of compounds 34-38 covering A1 = L = S

3. claims: 6(completely); 1, 2, 7, 8, 10-15(partially)
compounds of formula (I) covering A1 = S, L = single bond

4. claims: 3(completely); 1, 2, 7, 8, 10-15(partially)
carboxamides of formula (I) covering A1 = O

5. claims: 1, 2, 7, 8, 10-15(all partially)
compounds of formula (I) covering A1 = S, L = NH

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2017/055898

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
CN 102653619	A	05-09-2012	NONE
