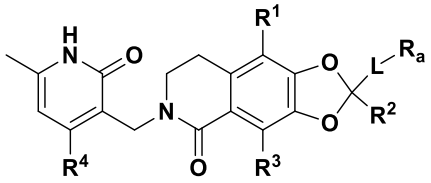
CLAIMS

[Claim 1]

A compound selected from the group consisting of dioxoisoquinolinone derivative compounds of the following Formula 1a, a pharmaceutically acceptable salt, an optical isomer, a hydrate and a solvate thereof :

[Formula 1a]



wherein, in Formula 1a,

R^1 is H, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkenyl, nitrile, aryl, a 5 to 6-membered aromatic heterocyclyl comprising 1 to 3 heteroatoms independently selected from a group comprised of N, O and S, or an aliphatic heterocyclyl including or not including unsaturated bonds in parts of a 5 to 6-membered ring, wherein the ring comprises 1 to 2 heteroatoms selected independently from a group comprised of N, O and S;

The C_{3-6} cycloalkyl, C_{3-6} cycloalkenyl, aryl, or a 5 to 6-membered aromatic heterocyclyl comprising 1 to 3 heteroatoms independently selected from a group comprised of N, O and S, or an aliphatic heterocyclyl including or not including unsaturated bonds in parts of a 5 to 6-membered ring, wherein the ring comprises 1 to 2 heteroatoms selected independently from a group comprised of N, O and S, is substituted or unsubstituted by 1 to 3 selected independently from the following group A;

L is a bond or C_{1-6} alkylene;

R_a is a substituted C_{5-9} bicycloalkyl;

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

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

R^4 is C_{1-6} alkyl, C_{1-6} alkoxy or thio-C_{1-6} alkyl;

Group A comprises halogen, C_{1-6} alkyl, C_{1-6} alkoxy, a 5 to 6-membered aliphatic heterocyclyl whose ring comprises 1 to 2 heteroatoms independently selected from a group comprised of N, O and S, wherein the C_{1-6} alkyl, C_{1-6} alkoxy and a 5 to 6-membered aliphatic heterocyclyl are substituted or unsubstituted with 1 to 3 selected independently from the

following Group B;

Group B comprises halogen, C_{1-6} alkyl, C_{1-6} alkoxy, a 5 to 6-membered aliphatic heterocyclyl whose ring comprises 1 to 2 heteroatoms independently selected from a group comprised of N, O and S, wherein the C_{1-6} alkyl, C_{1-6} alkoxy and a 5 to 6-membered aliphatic heterocyclyl are substituted or unsubstituted with 1 to 3 selected independently from the following Group C; and,

Group C is halogen, C_{1-6} alkyl, or a 5 to 6-membered aliphatic heterocyclyl whose ring comprises 1 to 2 heteroatoms independently selected from a group comprised of N, O and S.

[Claim 2]

The compound of Claim 1, wherein

R_a is a substituted bicyclo[2.2.2]octyl.

[Claim 3]

The compound of Claim 2, wherein

the substituted bicyclo[2.2.2]octyl is substituted by NR^5R^6, where the R^5 and R^6 are, respectively and independently, H or C_{1-6} alkyl.

[Claim 4]

The compound of Claim 1, wherein

R^1 is H, halogen, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{3-5} cycloalkyl or C_{3-5} cycloalkenyl.

[Claim 5]

The compound of Claim 1, wherein

R^2 is methyl.

[Claim 6]

The compound of Claim 1, wherein

R^3 is methyl or halogen.

[Claim 7]

The compound of Claim 1, wherein

R^4 is methyl, propyl, methoxy or thiomethyl.

[Claim 8]

The compound of Claim 1, wherein the compound of Formula 1a is selected from the

group consisting of the following compounds:

9-chloro-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

9-chloro-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer A;

9-chloro-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer B;

9-chloro-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-6-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2,4-dimethyl-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

9-chloro-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-6-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2,4-dimethyl-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer A;

9-chloro-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-6-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2,4-dimethyl-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer B;

9-chloro-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-6-((6-methyl-4-(methylthio)-2-oxo-1,2-dihydropyridin-3-yl)methyl)-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

9-chloro-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-6-((6-methyl-4-(methylthio)-2-oxo-1,2-dihydropyridin-3-yl)methyl)-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer A;

9-chloro-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-6-((6-methyl-4-(methylthio)-2-oxo-1,2-dihydropyridin-3-yl)methyl)-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer B;

9-bromo-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

9-bromo-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-

(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer A;

9-bromo-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer B;

9-cyclopropyl-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

9-(cyclopent-1-en-1-yl)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

9-cyclopentyl-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-9-vinyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-9-ethyl-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4-dimethyl-9-(prop-1-en-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-9-isopropyl-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-9-ethnyl-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4,9-trimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4,9-trimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer A;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4,9-trimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one isomer B;

2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-6-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2,4,9-trimethyl-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,4,9-trimethyl-6-((6-methyl-2-oxo-4-propyl-1,2-dihydropyridin-3-yl)methyl)-7,8-dihydro[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

4-chloro-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2,9-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

4,9-dichloro-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-2-methyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one; and

9-chloro-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(4-(dimethylamino)bicyclo[2.2.2]octan-1-yl)-4-methyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one.

[Claim 9]

A compound selected from the group consisting of dioxoisoquinolinone derivative compounds, a pharmaceutically acceptable salt, an optical isomer, a hydrate and a solvate thereof, characterized in that it is selected from a group comprised of the following compounds :

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-9-(furan-2-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(thiophen-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(pyridin-4-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-9-(6-fluoropyridin-3-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(1-methyl-1H-pyrazol-4-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(5-methylfuran-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(5-methylthiophen-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(pyridin-3-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(pyrimidin-5-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(1-methyl-1H-pyrrol-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(thiophen-3-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(thiazol-5-yl)-7,8-dihydro-[1,3]dioxolo[4,5-

g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-9-(1H-imidazol-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-9-(furan-3-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-2-(trans-4-aminocyclohexyl)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-9-(furan-2-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

(R)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-9-(furan-2-yl)-2,4-dimethyl-2-(trans-4-(methylamino)cyclohexyl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one; and,

(S)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one.

[Claim 10]

A compound selected from the group consisting of dioxoisoquinolinone derivative compounds selected from the group comprised of the following compounds, a pharmaceutically acceptable salt, an optical isomer, a hydrate and a solvate thereof:

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(thiophen-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(pyridin-4-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-9-(6-fluoropyridin-3-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(5-methylfuran-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(5-methylthiophen-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(pyrimidin-5-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(1-methyl-1H-pyrrol-2-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H pyrrol)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-2,4-dimethyl-9-(thiophen-3-yl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-9-(1H-imidazol-1-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-(trans-4-(dimethylamino)cyclohexyl)-9-(furan-3-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one;

2-(trans-4-aminocyclohexyl)-6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-9-(furan-2-yl)-2,4-dimethyl-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one; and,

6-((4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-9-(furan-2-yl)-2,4-dimethyl-2-(trans-4-(methylamino)cyclohexyl)-7,8-dihydro-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one.

[Claim 11]

A pharmaceutical composition comprising as an active ingredient the compound of any one of Claims 1 to 10 or a pharmaceutically acceptable salt thereof.

[Claim 12]

The pharmaceutical composition of Claim 11 for use in therapy~~, which is for a use is to treat cancers or tumors which can be treated by inhibiting EZH1 (Enhancer of zeste homolog 1) and/or EZH2 (Enhancer of zeste homolog 2) enzyme activity~~.

[Claim 13]

A pharmaceutical formulation comprising the pharmaceutical composition of Claim 11.

[Claim 14]

The pharmaceutical formulation of Claim 13, which has a form of a tablet, a pill, a powder, a capsule, a syrup or an emulsion.

[Claim 15]

The pharmaceutical formulation of Claim 13, further comprising one or more members selected from the group consisting of a pharmaceutically acceptable carrier, an adjuvant and a vehicle.

[Claim 16]

A use of the compound according to any one of Claims 1 to 10, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treatment of cancer or tumors, which can be treated by inhibiting EZH1 (Enhancer of zeste homolog 1) and/or EZH2 (Enhancer of zeste homolog 2) enzyme activity.